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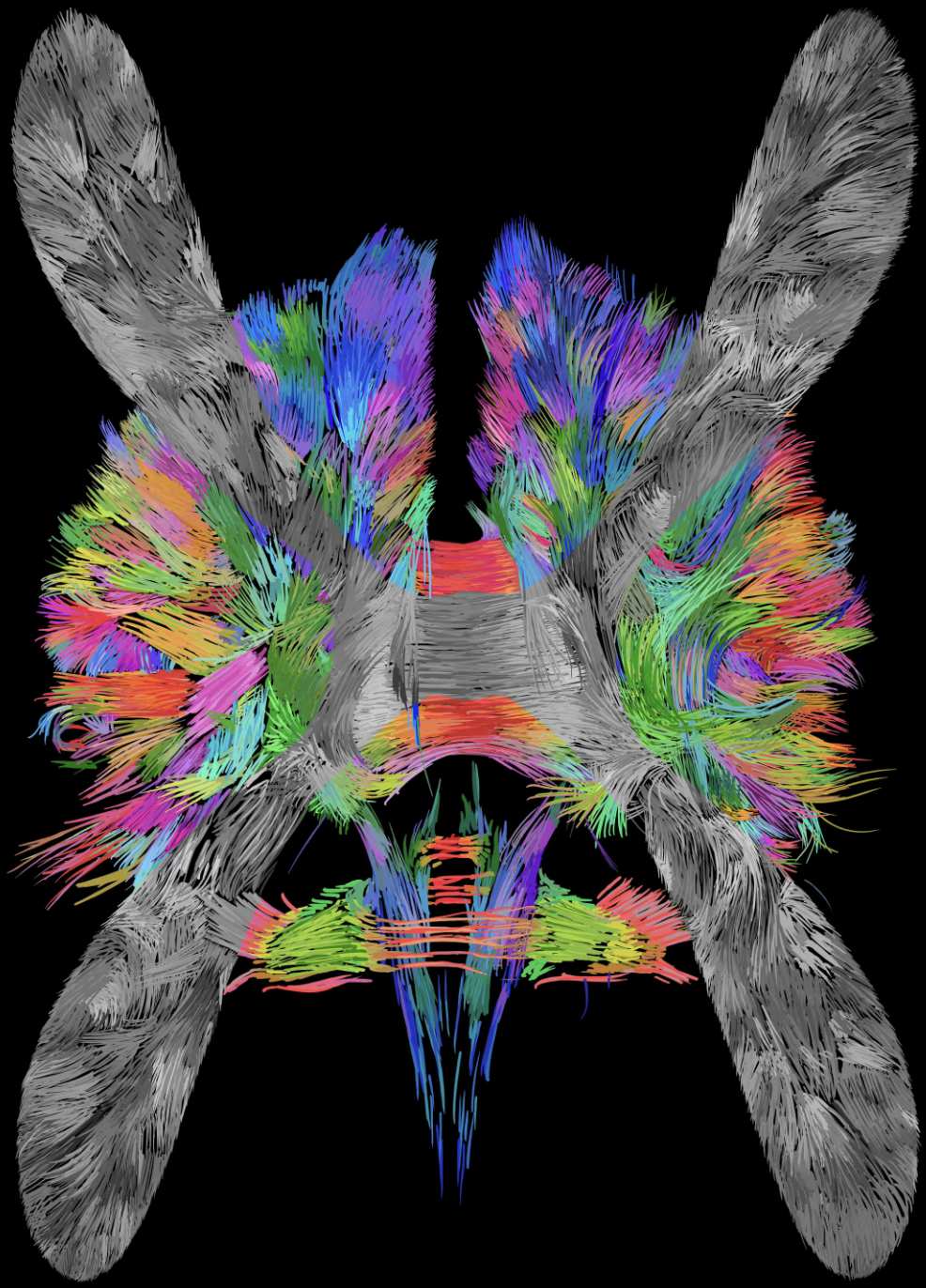

The Cognitive Model of Depression: Its evolutionary journey

Views of European Clinicians: medical assistance in dying

Consciousness and Computational Psychiatry

Genomics and Connectomics

Cover art by Alex Dawson

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In this issue of the Neurosphere Student Journal

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Welcome to the third volume of Neurosphere!

We are proud to present you with original research publications written and peer-reviewed by our very own students. The research articles survey, condense, and critically assess the current literature concerning 'the living mind' within recent years. While it may seem peculiar at first glance, this theme represents the change in our perception of the brain, its biochemistry and our relationship with our own minds. Reading these articles will broaden your perspectives, as we invite you to take a journey with us, where present and past collide, offering you a glimpse of our future.

Publications in this article include subjects ranging from computational psychiatry and artificial intelligence, to the evolution of cognitive models of depression, questions of consciousness, as well as an overview of the Human Connectome Project. One student has also written a comprehensive systematic review on The Views of European Clinicians on Medical Assistance in Dying and the factors that influence them which asks new questions from different perspectives into viewing medical death and afterlife.

We have put a lot of effort into bringing you high quality and compelling publications so we hope you enjoy it!

Contents

Research

Consciousness and Computational Psychiatry 1
Diyya Abdullah

The Views of European Clinicians on Medical Assistance in Dying and the factors that influence them: a Systematic Review of Literature 13
James Madden

The Cognitive Model of Depression: A Retrospective and Prospective View of Its Evolutionary Journey 30
Ebru Ozkazman

The 13-year Trek: Completion for Genomics and Momentum for Connectomics 37
Wing Gee Shum

Perspective

The State of Undergraduate Research Training 46
Daniel Shao

About the Neurosphere Student Journal

Our Neuroscience Society i

Joining Our Team ii

Publishing With Us iii

March 2023 | Vol.3 No.1

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RESEARCH

Consciousness and Computational Psychiatry

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Abstract

The computational theory of mind (CTM) dictates the human mind is a computational system and its cognitive functions are a practice of computation. This theory has grown into the misconception that the human mind is analogous with a computer. The reductionist nature of CTM obscures our perception of the mind and approaches towards confronting mental disorders. This review brings together studies examining computational systems such as artificial intelligence (AI) and neural networks to investigate their potential and limitations in the treatment of psychiatric disorders. In addition to this, the capacity of these systems for qualities unique to humans (such as: free will, suggestibility and subjectivity) will also be assessed.

Introduction

To understand the computational theory of mind (CTM) and its applications, we must first outline the history of the mind as a concept. For centuries, the nature of the human mind has been discussed and debated by philosophers, psychologists, and lay people alike, with varying theories regarding the mind's location and composition. The recent idea of the mind as a computing system appears outlandish when compared to the earlier understanding of the mind. An outline of the history of the mind as a concept is required to understand the progression of this concept from its primary discussions regarding its location and composition to its more recent debates regarding functional nature. In Ancient Greece, the great minds of Plato and Aristotle debated the nature of the mind's origins. Whilst Plato argued the mind was akin to a 'tabula inscripta,' Latin for 'inscribed tablet,' and possessed innate knowledge of the world, Aristotle claimed the mind was a 'tabula

rasa,' a scraped (clean) tablet, in possession of no prior knowledge. Furthermore, the location of the mind proved to be just as controversial as the nature of its beginning. Plato, influenced by Alcmaeon of Croton, accepted the brain as the centre of the mind (Celesia, 2012); however, Aristotle defined the brain as a cooling system for the heart, which he viewed to be the true seat of the mind. (Aristotle, 1829/1912, pp. 652a-652b) (Brandt Huppert, 2021). The divergent opinions of these two philosophers regarding the location of the mind served as the start of the cephalocentric versus cardiocentric debate, with Plato's views supporting the former and Aristotle the latter. Through time, arguments within cephalocentrism shifted towards identifying which specific areas of the brain were responsible for mental functions. Claudius Galen, a Greek physician and philosopher, proposed that the soul flowed through the ventricles of the brain and carried out the higher mental functions, based on his findings from animal dissections (Rocca, 1997). Galen's views dominated the field of human anatomy for approximately a millennium and a half before being denounced by the anatomist Andreas Vesalius. Vesalius' critique of Galenism and efforts in steering anatomy and medicine towards the use of human dissection initiated a scientific revolution (Splavski et al., 2019). Human dissection allowed for a better understanding of brain anatomy and physiology. Despite such advancements, there still was no agreement on the true nature of the mind or its location. The consensus, however, was the human mind was of a different nature than the human body; a theory known as mind-body dualism. The French polymath, Rene Descartes, is regarded as establishing the modern form of mind-body dualism. Influenced by Plato's dualism, Descartes agreed the mind was of a separate nature than the body but argued there had to be a point of interaction between them. He deduced this interaction lay within the brain, given scientists of the late 16th century had identified the brain as the organ responsible for voluntary movements and processing sensory information. Descartes then hypothesised the interaction point was singular to avoid seeing or hearing double and small enough to be easily set in motion by the mind (Finger, 1995). He thus concluded the pineal gland to be the interaction point, qualifying as a small unitary structure with limited mobility; 'all other parts of our brain are double,' he wrote in Article 32 of Passions of the Soul (1649/2015, p. 208). The 20th century also marked the start of neuroscience as a distinct field Cartesian dualism was heavily criticised by individuals such as British philosopher Gilbert Ryle, who described it as the dogma of 'the ghost in the machine.' To Ryle, the mind could not be separate from the body and to claim so would be a 'category mistake' biological processes and 'monism' was adopted as the scientifically accurate view (Ryle,2000, pp. 23–24). From the neuroscientific perspective, the mind was composed of. However, complex cognitive processes such as reasoning and thought were yet to be fully understood. The start of the mind being viewed as an entity arising from the brain and acting to 'compute' problems can be linked back to neuroscientist Warren McCulloch and logician Walter Pitts. In 1943, these two scientists proposed the mind and nervous system could be defined by propositional logic. Propositional logic is the field of mathematics concerned with the study of propositions (mathematical declarations that can be categorised as true or false) and the mathematical relations between combined

propositions. McCulloch and Pitts equated the 'all or none' activity of neurons with propositional truth values (true/false) and used the requirement of adequate stimulus for action potential firing as the basis of the proposition (Mcculloch Pitts 1990). McCulloch and Pitts' work was not the first mathematical work done on neural networks; however, it is regarded as the first approach to the modern computational theory of mind. In contrast to Alan Turing, who is often associated with this theory and likening the mind to a 'digital computing machine,' McCulloch and Pitts were the first to succeed in establishing their theory with a mathematical base (Piccinini, 2004). McCulloch and Pitts used discrete mathematics rather than the continuous mathematics employed in other attempts (Rashevsky, 1938) to represent nervous activity in mathematical models. Unlike continuous mathematics, which focuses on limits, discrete mathematics is focused on the use of whole numbers in counting and algebra. The use of discrete instead of continuous mathematics meant McCulloch and Pitts could lay out the mathematical foundation of their theory using logic and computation theory rather than limit themselves to differential and integral equations (Piccinini, 2004). This representation of the neural connections in computation was carefully designed to be as biologically true as possible. The translation of 'all or none' to 'true or false' was capable of accurately depicting nervous activity. This is because the physiological relations between nervous activities were able to be accurately represented in their respective logical propositions. Despite this, two problems challenged the McCulloch-Pitts neuron model (MP neuron model). The first was facilitation and excitation, where the responsiveness of neurons undergoes temporary changes; and the second of which was learning, where antecedent activity causes permanent alternations in responsiveness. To overcome these difficulties, McCulloch and Pitts proposed a net whose responsiveness is altered could be substituted with an equivalent net with fixed responsiveness. Both authors admitted this formal equivalence where synaptic plasticity was disregarded could not be taken as a factual explanation; however, they emphasised the importance of this representation in showing changes that cause facilitation, extinction, and learning do not affect the correspondence of neuronal propositions to logical propositions. In this manner, one of the key flaws of CTM was demonstrated; its agnosticism towards cardinal qualities of the human mind, ie neuroplasticity and the perpetual capacity for change (McCulloch Pitts 1990). The work of McCulloch and Pitts served as the foundation for the computational approach to neuroscience. Fifteen years following McCulloch and Pitts's 'Logical Calculus Of Ideas Immanent In Nervous Activity (1943),' American psychologist Frank Rosenblatt assembled the first physical manifestation of an artificial neural network (ANN) known as the Perceptron (Rosenblatt, 1958). The Perceptron was inspired by the MP neuron model but was an advancement from the limited nature of MP neuron models in its input-output capability. The MP neuron model, as mentioned previously, receives only Boolean (true/false) inputs whilst the Perceptron is capable of reviewing various inputs. In addition to the increased scope of inputs, the Perceptron can 'weight' these inputs to have a greater or lesser impact on the output given and Perceptrons can be organised into hierarchical layers to contribute towards decision-making of a higher sophistication. This increase of variety and 'weighting' of inputs rendered the Perceptron

superior to the MP neuron model in terms of similarity to the human mind. This encouraged further attempts at representing the mind in such computational models and brings us to one of the main models this review aims to investigate: Artificial Intelligence. The end of the 1960s was also the starting point of Artificial Intelligence (AI) which was first proposed by computer scientist and professor, John McCarthy, in 1956. However significant progression of McCarthy's concepts was not seen until the early 21st century due to financial and technological barriers to AI advancement One of the key necessities to the progression of AI was the Graphic Processing Unit (GPU). GPUs, invented in 1999, work to process large quantities of data simultaneously by hundreds of small processor cores that carry out parallel computation by breaking down complex calculations into thousands of smaller steps (Suchard et al., 2010). It was only until the increase in GPU affordability and higher storage capacities became more accessible that the field of AI underwent significant developments (Jones et al., 2018). Today, machine learning (ML) is considered as the most notable of AI abilities. In ML, computer algorithms are taught how to accomplish a task rather than being instructed to do so. In the case of these algorithms, the data 'teaches' the machine what accounts for a satisfactory answer rather than explicit programming. ML is also responsible for the resurgence of ANNs and their use in 'Deep Learning' (Nichols et al., 2018). Deep learning ANNs take advantage of the increase in power provided by GPUs to process enormous data sets in significantly short periods of time (Jones et al., 2018). A subset of ML, Reinforcement Learning (RL), consists of AI systems learning through trial and error (Janiesch et al., 2021). As RL is an unsupervised example of ML, the feedback received does not contain the correct answer to the problem; thus, the system must learn from previous mistakes and gain intelligence in a similar manner to humans. Today, RL has found its way into the budding field of computational psychiatry. Computational psychiatry is a field which concerns itself with the representation of the relationships existing between neurobiology, the brain's environment, and mental symptoms in computational models.These models are designed to capture cognitive processes and provide a new perspective on mental function and subsequently, dysfunction (Adams et al., 2016). Three main control systems exist within RL: model-based, model-free, and Pavlovian (Montague et al., 2012). Both model-based and model-free control systems attach decisions to affective consequences (changes in mood/self-esteem that occur as a result of attributional processing) whilst the Pavlovian control system focuses on utilising positive and negative reinforcement to ensure the system continues to improve itself whilst computing problems. The idea of negative and positive reinforcement in Pavlovian RL is based on classical and operant conditioning mechanisms used in psychology with the only difference being the substitution of punishments with less reinforcement (less reward). These three types of RL have been employed in the computational modelling of mood disorders with the most notable being depression (Montague et al., 2012). RL models are also capable of providing a computational interpretation of uncontrollability and the feeling of 'learned helplessness' that is associated with certain forms of anxiety and depression (Seligman, 1975) (Montague et al., 2012). The ability of RL to capture phenotypes of human cognitive functions

and dysfunctions in computational models is thought of as the promising start to understanding and defining mental disorders with a higher level of accuracy.The collected phenotypes are then linked with possible neural and genetic causes to catalogue the presentation of these disorders; thus, enabling deeper investigations into the biological causes of these disorders and the potential movement away from cluster symptom-identification as the main diagnostic tool in psychiatry. This review aims to investigate the limitations and reductionist nature of computational psychiatry, (2) investigate the potential of computational psychiatry in treating psychiatric conditions, and (3) assess the capacity of computational systems such as AI/neural networks for qualities unique to the human experience (free will, suggestibility, and subjectivity).

Method

Data for this review was collected via the PubMed, Springer and ScienceDirect databases, using the advanced search tools to narrow search results to key terms (listed below). As this subject holds a significantly rich history of development, texts from the last century were also considered for their historical significance. The compilation of these texts was undertaken in a chronological manner to create a timeline of the history of the mind as a concept and the subsequent events that led to the development of computational psychiatry. To provide a better understanding regarding the philosophical and historical contexts of this subject, a selection of books were also used. These books were reviewed in terms of their credibility by fact-checking claims via credible sources, i.e. peer-reviewed journals in respective fields (The Philosophical Review, Mind, and Journal of Philosophy). Certain non-factual claims are used within the review to showcase the development of ideas within this field, and such claims are corrected later in the text. The key words below were separated according to topic and used accordingly with the database deemed most relevant; eg, papers on 'Neurophilosophy of Mind' were retrieved via The Philosophical Review, Mind, and Journal of Philosophy. Over 40 sources were initially retrieved; however, approximately 20-25 sources were selected from the initial sources. This selection was based on scientific significance and historical significance. Sources relating to 'Computational Psychiatry' and 'Computational Neuroscience' with experimental evidence were prioritised over those without experimental evidence. Sources pertaining to the historical aspect of this review were categorised according to their relevance and influence on the field of neuroscience.

Key words and phrases

'History of Mind,' 'Concept of Mind,' 'Computational Neuroscience,' 'Cognitive Neuroscience,' 'Computational Theory of Mind (CTM),' 'CTM limitations,' 'Connectionism,' 'Neurophilosophy of Mind,' 'Cardiocentrism,' 'Dualism,' 'Artifical Intelligence,' 'Neural Networks,' 'Artificial Neural Networks,' 'Propositional Logic,' 'Discrete Mathematics,' 'GPU programming,' 'Deep Learning,' 'Computational Psychiatry,' 'Neurobiology,' 'Machine Learning,' 'Behaviour,' 'Affective Control,' 'Subjectivity of Mind,' 'Free Will and the Mind,' 'Neuroscience of Consciousness,' 'Conditioning,' 'Computational Models,' 'Future

of Computational Psychiatry,' 'Computational Psychiatry Limitations.'

Results

The results obtained from the review of existing literature regarding computational psychiatry and its applications emphasised the gap between biological psychiatry and neuroscience (Montague et al., 2012). Most studies were centred around the same disorders: depression, anxiety, and schizophrenia (Adams et al., 2016; Huys et al., 2021; Montague et al., 2012; Rutledge et al., 2019;). These studies focused on the modelling of aberrant decision-making and valuations associated with these disorders into computational forms (Adams et al., 2016; Montague et al., 2012). Most studies focused on data-driven approaches of computational psychiatry, namely, the use of machine learning, (Chekroud et al., 2016; Gillan et al., 2016; Huys et al., 2021; Montague et al., 2012) whilst other studies advocated for a combination of data-driven and theory-driven approaches (Huys et al., 2016; Rutledge et al., 2019). Studies incorporating machine learning primarily utilised reinforcement learning (RL) models rather than deep learning (DL) (Chekroud et al., 2016; Montague et al., 2012) to understand the characteristics of certain disorders in better detail. For example, data collected from the observation of animals indicates serotonin release may have in involvement in Pavlovian learning and subsequently, the prediction of aversive consequences (Dayan Huys, 2009). This potential involvement in Pavlovian learning inspired computational modelling on the basis of subjects not explicitly needing to learn what not to do in future problems. Another example of a RL model can be observed in understanding learned helplessness in depression and anxiety. In such cases, animals were conditioned into learned helplessness through uncontrollable punishments and rewards. This caused the animals to learn they cannot accurately predict outcomes of a situation based on their actions. When placed in a new environment, these animals do not attempt to explore nor escape due to the learned unpredictability of the outcomes of their actions. The computational interpretation of this characteristic incorporates Bayesian approaches (a statistical approach to predicting the likelihood of an event based on available evidence) to quantify the relationship between the animals' prior probability distribution over the potential future environments. Prior distributions were noted to offer substantial understanding of developmental and adult behaviour, but no further detail was given to link this understanding to its application in treating such learned helplessness behaviour (Adams et al., 2016; Montague et al., 2012). In addition to understanding specific characteristics of depression, it was also found a computational approach could be used in the prediction of treatment outcome for patients with depression. Chekroud et al. (2016) successfully built a machine learning model to predict the treatment outcome of patients with depression given Citalopram. 25 predictive features were used to train a machine-learning algorithm in predicting clinical remission. The study used a combination of several weakly predictive models to develop a gradient boosting machine rather than linking one strong model to a data set which enabled the model to identify data that previous models failed to predict: thus, increasing the accuracy of the model. The performance of this model was on par with disease risk, recurrence, and treatment outcome calculators in medical

areas such as oncology and cardiovascular disease. In addition to depression and anxiety, attempts have also been made to characterise schizophrenia in computational terms.

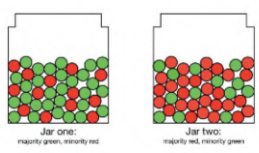

Figure 1a – Psychology experiment illustrating precision imbalance
An observer is shown two jars; the first, with many green beads and few red beads; the second, with many red beads and few green beads.

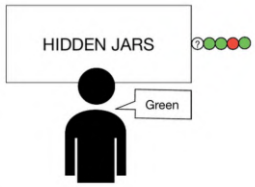

Figure 1b – Psychology experiment illustrating precision imbalance
The jars are hidden and a string of beads is drawn out. The observer is instructed to guess the next bead in the sequence. In this instance, the observer is made to believe the beads are being drawn from the jar containing the most green beads (jar one) and thus, guesses the next bead is green.

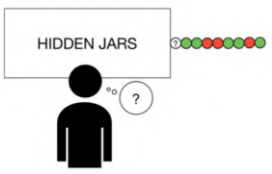

Figure 1c – Psychology experiment illustrating precision imbalance
The next sequence drawn displays an equal number of green and red beads. This confuses the observer and makes it difficult to guess the next bead in the sequence.

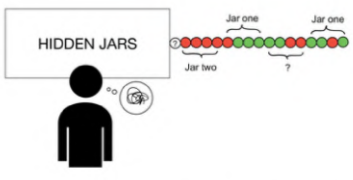

Figure 1d – Psychology experiment illustrating precision imbalance
Two more sequences are drawn. The observer is initially led to believe the beads are being drawn from jar one from the start of the sequence; however, the end of the sequence makes the observer believe the beads are being drawn from jar two. Consequently, volatility arises and the observer suspects the jars have been switched between each turn.

Adams et al. (2016) attempted to liken the hallmark feature of schizophrenia, 'jumping to conclusions,' to the outcome of precision imbalance in a hierarchical model. A classic psychology experiment which embodies this precision imbalance is referenced to showcase this link [Figures 1a 1b, 1c and 1d]. In this experiment, an observer is shown two jars of different coloured beads. One of the jars contains mainly green beads and a few red beads. The other jar contains mainly red beads and a few green beads. Both jars are hidden, and the observer is shown a short sequence of beads with the task of guessing the next bead in the sequence. At first, the short sequence may make it seem as if the next bead is green. More beads are drawn each turn, and the resultant sequence appears with almost equal amounts of green and red beads, rendering the observer uncertain of the next bead in the sequence. Upon the next drawing of more beads to the sequence, the observer notices an increase in green again. In the final turn, all beads in the sequence are red. In such instances of temporal changes, 'volatility' arises, and the observer suspects the jars have been switched between each turn. This example is used to demonstrate what occurs when the precision at the bottom of the hierarchical model is too high in comparison to that of the top; that is, the model does not process the outcome of a sensory prediction error as a result of chance and instead, assumes change in the environment (tampering). Thus, Adams et al. (2016) proposed this precision imbalance could be attributed to delusion formation common in cases of schizophrenia. The main cortical abnormalities of schizophrenia, hypofunction of the glutamate receptor known as N-methyl-D-aspartate receptor (NMDA-R), reduced γ-Aminobutyric acid (GABA) synthesis,

and hypoactivation of Dopamine-1 (D1) receptors in the prefrontal cortex (PFC), are thought of as to reduce synaptic gain in the PFC and hippocampus (HC) (Adams et al., 2016). Synaptic gain (and the loss of it) is represented as the equivalent of precision in precision imbalance. This is justified by the comparison of Bayesian inference, where precision dictates the influence of certain information on another, to neural message passing, where synaptic gain dictates the influence of one neural population on another. As a result, a loss of synaptic gain is represented as a loss of precision in the computational model, with a subsequent loss of the model's relatively more abstract priors over relatively more concrete sensory information. This loss would then render the environment more unpredictable and uncertain akin to how patients with schizophrenia perceive the world and display hyperattention to sensory stimuli as a result. Adams et al. (2016) theorised this may be similar to the central coherence of autistic people; with a difference in the onset of precision loss explaining why, although both persons with autism and schizophrenia display difficulties in understanding the mental state of others, only the latter attributes mental states to others. Theory-driven approaches such as artificial neural networks were also found to have first been successfully applied in other areas of medicine in the late 1990s and demonstrated a wide array of success in various areas of clinical diagnosis such as appendicitis, myocardial infarction, and biopsy specimen examinations (Baxt, 1995). Although the use of data-driven approaches of computational psychiatry appeared to be the most favoured, certain studies pointed out the weakness of using data-driven approaches alone. These studies emphasised the agnostic manner of data-driven analyses to the nature of the data being analysed such as the potential of these algorithms to neglect already established facts regarding the structure of the data collected. The combination of data-driven and theory-driven approaches was argued to compensate for this weakness as theory-driven algorithms act to recover sufficient statistics of which data-driven algorithms do not (Huys et al., 2016; Rutledge et al., 2019). Lastly, all studies identified the complexity of the human brain and the environment it interacts with as one of the biggest obstacles in the progression of computational psychiatry. In search of literature to better understand the complexity of mental disorders, it was found psychiatric conditions worsen with time and in respect to the advancement of modern society. This was particularly eminent in a study where Ugandan members of a hunter-gatherer lifestyle were relocated into Western society and experienced a significant worsening of previous psychiatric conditions (Hidaka, 2012). To summarise, results demonstrated a variety of different ways to view mental disorders from a computational viewpoint. One study, Chekroud et al. (2016), showed the use of computational models in predicting treatment outcome. Despite these findings, no literature showing the direct application of these models in the treatment of psychiatric disorders.

Discussion

The key aim of this review was to highlight and showcase the limitations of computational representations of the human mind. Results obtained from the conducted literature review demonstrate a number of successful applications of CTM in understanding psychiatric disorders from a different perspective. The content

matter regarding these disorders, however, is minimal and most of the available literature echo the same results from the same select real-world applications of the computational models developed. The majority of literature also focuses on the same disorders: depression, anxiety and schizophrenia (Adams et al., 2016; Huys et al., 2021; Montague et al., 2012; Rutledge et al., 2019;). Although these studies successfully captured characteristics of these disorders in computational terms (Adams et al., 2016; Montague et al., 2012), they failed to contribute to the development of new or more efficient treatment means for these disorders. The most notable progress was achieved by Chekroud et al. (2016) whose application of computational modelling displayed the potential to reduce the time required for a patient with depression to be matched with an effective treatment. This model, however, was developed to assess the outcome of patients achieving symptomatic remission by the administration of Citalopram and would require significant expansion and development to predict treatment outcome for the wide array of other available anti-depressants in use. This is disregarding other forms of treatment such as cognitive behavioural therapy (CBT), interpersonal psychotherapy, problem solving therapy (PST) and psychodynamic therapy (Cuijpers et al., 2019) which would require an alternative predictive model due to the difference in treatment nature. These treatments would also be significantly harder to predict outcomes for due to the increased influence of subjectivity variation from individual to individual which makes setting predictive features more challenging. The applications of computational approaches appear to be successful in most areas of medicine other than psychiatry. This can be explained by the significant influence of subjectivity in mental disorders as opposed to physical ailments. Where diagnostic criteria for the majority of somatic disorders is somewhat set and defined, diagnostic criteria for psychiatric conditions are prone to overlap and are loosely defined. In addition to this, the field of computational psychiatry is heavily reliant on diagnostic systems widely acknowledged as inadequate and flawed, such as the Diagnostic and Statistical Manual (DSM) (Khoury et al., 2014; Kutchins Kirk, 1986; Wakefield, 2015). For the field of computational psychiatry to obtain an accurate set of data to use as a foundation other than the DSM, large samples of data would need to be recategorised and assessed The greatest limitation central to all other issues in the field is time. In the hypothetical scenario, completely accurate, reliable data was available the time required to compile this data and the time required to incorporate it into computational models would still cause a significant hindrance in the progression of the field. Although one could argue data collection could be sped up by the use of computer databases or large-scale surveys, the correct use of this data in its computational context could only be carried out by individuals with adequate knowledge of mathematics, neuroscience, psychiatry, pharmacology, computer science and engineering. It is the integration of these fields that gives computational psychiatry its unique viewpoint on psychiatric disorders, but also acts as a limitation. The most efficient way to overcome this problem would be to devise 'teams' of researchers from their respective fields to undertake multidisciplinary collaboration; this solution too, is limited by quantity. All studies acknowledged the complexity of the brain and the environment it interacts with as one of the

greatest obstacles of the field and as an obstacle that will only continue to grow in complexity as the field itself progresses. For computational psychiatry to progress, technology must progress too. The progression of technology does not come without the progression of society. It has been shown that psychiatric conditions have advanced in complexity to societal and technological advancement (Hidaka, 2012). Those with simpler lifestyles, such as the Ugandan hunter-gatherer lifestyle, are subject to mental disorders of a simpler nature than those of in Western societies (Hidaka, 2012). The intricacies of today's psychiatric conditions may only be accurately captured in fifty years' time, in which case, it may seem impossible to model the disorders of that time. That is the case presented by computational psychiatry today, which has captured characteristics of disorders defined decades ago but has failed in developing effective treatments and interventions.

Conclusion

This study investigated the current applications of computational approaches to psychiatry which were initially influenced by the computational theory of the mind (CTM). The systematic review conducted displayed a limited number of real-world applications of proposed models. Although computational approaches appeared to be beneficial in understanding psychiatric disorders from a different perspective and, in one instance, predicting treatment outcome, they did not appear to show any scope for the development of new treatments for these disorders. Future directions for computational psychiatry could be the development of phenotype databases for psychiatric conditions to help both categorise symptoms and compile data regarding genetic, environmental, and societal factors. The development of the field as a categorising tool for 'disordered' psychiatric phenotypes depends upon its ability to keep up with the increasing complexity of mental disorders over time in modern society.

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RESEARCH

The Views of European Clinicians on Medical Assistance in Dying and the Factors that Influence Them

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Abstract

Medical assistance in dying is one of the most ethically contentious practices in healthcare globally. Across Europe, different degrees of legalisation are offered by their respective governments. The views of healthcare works are important for designing legislation, informing practice. They also add to a constructive debate around this topic, and thus characterising their views is essential work. Primary research articles describing healthcare worker's views of MAiD (medical assistance in dying) and how professional, personal, and situational factors influence them were systematically reviewed using a "snowballing" method. Research published within the past five years from any European country has been included. Overall, HCWs (healthcare workers) support the legalisation of MAiD. Support tends to increase when HCWs are younger, female, irreligious, or have more experience to palliative care. The patients HCWs are most likely to support MAiD on behalf of are older, experiencing significant suffering, have little hope of a cure or treatment, and have the capacity to make the decision. Many of the factors described in this review should be considered when designing healthcare systems to provide MAiD. Some of the difficulties associated with MAiD are intrinsic and irreducible, but others can be mitigated with systemic change and consideration of the views of the HCWs who provide MAiD, which is described briefly.

Introduction

MAiD refers to "a medical act where, on a voluntary request by a consenting person, a clinician either administers a substance, or prescribes a self-administered drug, to cause death"[1]. This is typically refined into its subtypes, euthanasia (where the healthcare practitioner administers the death-causing substance) or physician assisted suicide (PAS, where the patient takes the death-causing substance themselves).

MAiD remains a subject of controversy despite it's legalisation in a number of European countries and US states. Doctors hold widely varying opinions on it, which may impact it's practice. In addition, legal debates on the subject of MAiD often begin by characterising the opinions of the service providers likely to distribute it, which in this case are the opinions of doctors, nurses, pharmacists, social workers, and other patient-facing healthcare workers (hereafter referred to as 'HCWs'). Previous studies have outlined the importance of understanding the attitudes of healthcare providers as they should be accounted for when designing and applying legislation. They are also important as a starting point to examine how these attitudes may impact the patient's experience through the HCP-patient relationship. Finally, the views of HCWs, as industry professional, has some significant influence of the general public's support for these matters [2]. For these reasons, the characterisation of HCWs attitudes towards MAiD remains an important question.

Despite variations to some aspects of the legal criteria across different countries, all legal frameworks include stringent inclusion and exclusion criteria, the majority including some conceptions of intolerable suffering or pain, the terminal nature of the disease, lack of confounding mental health conditions/impaired judgment, and sometimes the requirement for repeated requests over a period of time (legal review in [3]). Recent reports have highlighted a dearth in volume and quality of research (Sleeman and Owen 2021) and physician engagement with research on this issue, making it difficult to quantify the attitudes of physicians towards MAiD. This review aims to address some of the limitations of previous studies by systematically reviewing the literature on HCWs attitudes towards assisted dying in European countries, focussing on whether they are positive or negative.

The last key study in this area was Patel et al. [1], which systematically reviewed the reactions of healthcare practitioners (HCPs) to legal requests for MAiD. It limited itself to countries where MAiD is legalised and only studies examining HCWs that had direct experience with it. This review aims to address these limitations by including these two criteria and including research conducted since its publication.

Method

A literature search was conducted between May and July 2022 using the PubMed database. The search terms used were combinations of the following: doctors, nurses, healthcare practitioners, clinicians, and euthanasia, physician assisted suicide, medical assistance in dying. The final search was 28th July 2022. The search

was limited to original peer-reviewed articles published in English between 1st of January 2017 and the 30th of April 2022. Additional relevant publications were identified using a "snowballing" method, by checking the reference lists of each included publication.

Both quantitative and qualitative studies were eligible for inclusion if they addressed the views of European patient-facing HCWs and characterised them at least as generally positive or negative. Articles studying laypeople were included as long as they had a HCW cohort, in which case only that was analysed. Studies from any European country were included.

Studies were excluded if they were not published in English, did not use primary data or did not use a descriptive or interpretive methodology. Grey literature was also excluded. Studies addressing topics other than requests for MAiD and those that did not focus on the perspectives of regulated healthcare professionals were also excluded.

A three stage process was used for extracting data from each article. The first stage extracted the procedural methods of the study, such as their methodology, included and excluded cohorts, and their statistical analysis methods. The second stage critically reviewed each paper with the analysis framework, which highlighted HCW- or patient-based factors that had been demonstrated to impact the HCWs views of MAiD. Finally, the identified factors were compared with the conclusions drawn by the article's authors. They were recorded as being relevant or irrelevant depending on each article's statistical analysis.

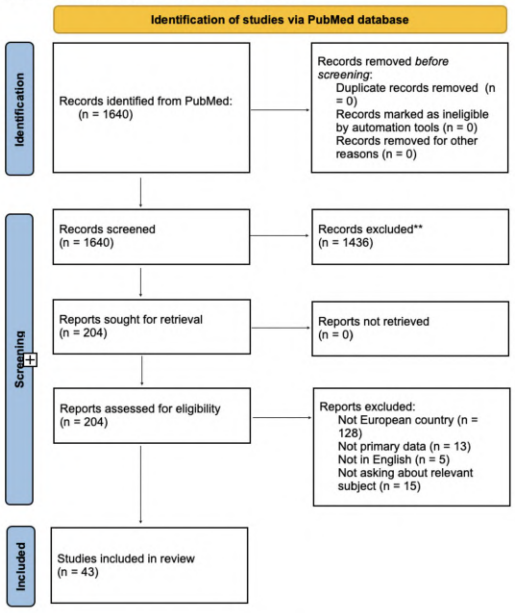
Data quality was assessed using standard quality criteria used by other reviews, which were the following factors, all of which needed to be clearly stated and well-defined:1) Research aims, 2) Study populations, 3) Study design/data collection methods, 4) Independent and outcome/dependent variables and 5) Statistical analysis (or, in the case of qualitative articles, balanced consideration of potential cofounders).

Results

Results

Study identification and refinement

Fig. 1. PRISMA diagram of our literature search process


Identification of studies via PubMed database
Identification
Records identified from PubMed: (n = 1640)
Records removed before screening: Duplicate records removed (n = 0) Records marked as ineligible by automation tools (n = 0) Records removed for other reasons (n = 0)
Screening
Records screened (n = 1640)
Records excluded** (n = 1436)
Reports sought for retrieval (n = 204)
Reports not retrieved (n = 0)
Reports assessed for eligibility (n = 204)
Reports excluded: Not European country (n = 128) Not primary data (n = 13) Not in English (n = 5) Not asking about relevant subject (n = 15)
Included
Studies included in review (n = 43)

3.2 Table 1: Study characteristics (N=43). This table identifies basic characteristics of the included studies, namely country of origin, study design, and professional cohort.

Study characteristics	No. of studies	% of total studies (n/43)
Country of investigation		
Austria	1	2
Belgium	10	23
Denmark	1	2
Finland	3	7
Germany	2	5
Greece	3	7
Ireland	1	2
Italy	1	2
Netherlands	14	33
Poland	1	2
Portugal	1	2
Sweden	1	2
Switzerland	3	7
UK	2	5
Publication year		
2017	5	12
2018	6	14
2019	12	28
2020	10	23
2021	7	16
2022	3	7
Study design		
Survey	32	75
Interview	8	19
Both of the above	1	2
Focus group	1	2
Case note review	1	2
Categories of HCW addressed		
Physician (medical)	20	47
Physician (surgical)	4	9
Physician (psychiatric)	14	33
Physician (outpatient e.g. GP)	11	26
Nurse	5	12
Students (medicine, pharmacy)	4	9

Included studies' characteristics

After refining, our literature search returned 43 papers that were included in our final analysis. A breakdown of the number of studies per country per profession is included in Table 1 (see Appendix 2 for an overview of the included studies and their broad demographic characteristics).

The analysis framework identified the factors that the included studies found significant (i.e. those that had some bearing on the views of HCWs on MAiD) and insignificant (i.e. the factors that had no such bearing).

I General attitudes

22 studies reported findings on HCWs general feelings towards a variety of MAiD practices, of which 11 were generally positive. The rest reported generally mixed (n = 5) or generally negative (n = 6) feelings. On the whole, the majority of HCWs support at least the principle of MAiD, believing there are some circumstances in which it is acceptable, despite their differin opinions on specific scenarios (e.g. the medical conditions in which it is appropriate). The percentage of physicians who support it ranges from 85% to just 25%, with the number of studies whose cohorts were overall in favour of MAiD skewing this variation positively.

II Professional factors of HCW

IIa Legal concerns

There are three legal concerns identified in the included articles. The first two are from ten Cate et al.:

1. Perceived legal criteria. This refers to physicians mistakenly taking a specific MAiD practice to be a legal requirement when it isn't, or vice versa.

2. Individual legal interpretations. This refers to

physicians having differing or idiosyncratic views of legal terminology.

The third is from Ntantana et al.:

3. General fear of legal action. This refers to a general sense of uncertainty physicians have when prescribing MAiD, based in concerns about litigation, leading to changes in practice.

These difficulties in understanding and applying legal criteria, and the concomitant fear of action, lead to disparities in prescription of MAiD: for example, Humbeeck, Piers [4] found that in a vignette scenario where "significant suffering is caused by a life-limiting medical condition [i.e. the Belgian legal criteria are unequivocally met]... only 50% of Belgian healthcare providers are aware of the existing legal basis for euthanasia in this case".

IIb HCW's specialty

10 studies reported that the specialty of the HCW affected the way they view MAiD practices and/or how they make decisions with patients who request it, whilst 1 study found this factor insignificant. There were three reasons that different specialties held broadly different views on MAiD. Firstly, disparity was due to how often different specialties are exposed to requests for MAiD; Jahn-Kuch, Domke [5] found that haemato-oncologists were asked for PAS "significantly more often than other physician groups", for example. Another contributing factor is the sorts of relationships different treatment settings engender; [4], for example, found that GP's spending more time with their patients than geriatricians led them to understand their condition and background more holistically, and were therefore more willing to prescribe MAiD.

Thirdly, the nature of illnesses treated by particular specialties meant that they were exposed to more contentious MAiD instances. In particular, approval of MAiD from psychiatrists was more polarised, mainly due to the difficulty in establishing whether a wish to die was caused by depression or other psychiatric illness, and whether psychiatric illnesses met definitions of intolerable or unbearable suffering defined in the legal criteria. For example, Pronk, Sindram et al. 2021a found that whilst psychiatrists have more knowledge in determining the pathological nature of a wish to die and mental competence, they tended to view the prescription of MAiD as outside the purview of psychiatry, making them less likely to prescribe it themselves. Elderly care physicians tended to the opposite conclusion; Evenblij, Pasman et al. 2019b found they found MAiD prescription more conceivable than other specialties.

IIc HCW-patient relationship

8 studies reported on the impact of MAiD practices on the HCW-patient relationship. In general, most reported that said impact was negative, either for the patient or the HCW themself. All of the studies that discuss this factor demonstrate it to be significant in forming a HCWs opinion of MAiD in general, and generally found it to negatively impact their views on MAiD. Verhofstadt, Audenaert [6], for example, found that only "half would consider a euthanasia assessment to be compatible with a therapeutic relationship", but that a third would be willing to engage in it regardless.

Pronk, Evenblij [7] describe two reasons MAiD

negatively impacts the HCW-patient relationship. The first is countertransference, which their psychiatrist interviewees defined as "identifying with the patient" and "to become part of a particular dynamic", and which "could interfere with the psychiatrist's ability to objectively consider a request for EAS [euthanasia and assisted suicide]". This was counteracted by independent consultation from colleagues and peers. Many also saw the goals of psychiatric treatment as incompatible with the goals of MAiD. Finally, emotional difficulties, including blackmail from patients, forms of control and direction from others, and time pressure around MAiD referrals were identified by Boer, Depla [8] as contributing to a toxic emotional HCW-patient relationship that negatively impacted the HCW's views of MAiD.

Broadly speaking, the longer and richer therapeutic relationships were, the less preferable MAiD was to clinicians, although the effect could also be positive; "Some GPs indicated that they felt responsible for their patients... a responsibility connected to their profession" [9]. Schuurmans, Bouwmeester [10] further develop these positive feelings; "emotions like heroism, being in control, satisfaction and relief were also mentioned... [respondents equated] this with the legitimation of the physician's power when having performed euthanasia". Overall the impact of the HCW-patient relationship on the clinician's views of MAiD in general are complex, and are dependent on the length and character of the relationship, and occasionally this leads to directly opposite outcomes by HCWs within the same profession and clinical setting.

IId HCW's prior experience with MAiD

Of the 8 studies that discuss the HCWs prior exposure to MAiD, 7 deem it significant. In general, increased exposure to MAiD requests and EOL care are robustly associated with the HCW supporting it. Three studies quantified this effect statistically: Brinkman-Stoppelenburg, Evenblij [11] found previous euthanasia experience was strongly correlated with a physician finding it conceivable (OR = 1.94; 95% CI = 1.21–3.12); Evenblij, Pasman [12] found much the same effect on univariate analysis. In addition, the same authors demonstrated more positive reactions to MAiD with repeated exposure; the odds ratios of finding euthanasia a burdensome process were lower in physicians who'd received three or more requests in the past year, compared to receiving none or up to two (OR 2.49 [1.15–5.39] and OR 2.58 [1.24–5.39] respectively [13]). Finally, while no statistics were performed for this finding in particular, Verhofstadt, Audenaert [14] found Belgian psychiatrists were more amenable (70%) towards MAiD assessment when they had received requests.

III Personal factors of HCW, IIIa Religiosity of HCW

Of the 17 studies that describe the impact of religiosity, 14 of them found it to be significant. Generally, a HCWs tendency to associate with an organized religion correlated with a less favourable attitude to MAiD practices. This was found to a number of degrees by different authors, such as Cleemput and Schoenmakers [15], who found that 50-81% of religious doctors were reluctant to perform euthanasia in early to late

stage dementia respectively, compare with 15-56% of their irreligious colleagues. Randwijk, Opsahl [16] found that religiosity predicted objections to MAiD with an OR of 1.57. One study identified Islam specifically as contributing particularly strongly to rejection of MAiD: "Being a non-believer is more strongly associated [with accepting MAiD]. [Medical students] from Muslim family backgrounds are particularly likely to disagree with actions that hasten death" [17]. The authors quantify this, showing that of the three religions respondents identified with (Christianity, Islam, and Hinduism), Muslim students had a lower agreement score than the other two religions on average (Christian: 15.4, Muslim: 12.1, Hindu: 14.7. In this study, participants answered how likely they were to agree to five particular MAiD scenarios on a five-point scale, so possible scores range from 5-25, with 25 indicating they strongly agreed with all of the MAiD interventions. Muslim students therefore have the lowest agreement with MAiD on average compared to the other two religions studied).

Piili, Metsänoja [18] reported that the influence of religion on physicians' engagement was much stronger in 1999 than in 2015, and Alminoja, Piili [19] found "religion had a stronger influence on ethical decisions among the GPs than it did among the students". These findings suggest that the influence of religion may intersect with other factors such as age, length of time in practice, and specialty. In addition, some physicians have personal moral values that prohibit MAiD outside of a formalised religion [20].

IIIb Age of HCW

Age was significantly associated with divergent views on MAiD by 9 studies and rejected by 3. Of the studies for whom age was significant, they largely agreed on the trend that older physicians tend to disapprove of MAiD or are unwilling to take part in it. Jahn-Kuch, Domke [5] found positive approval of PAS in 55.2% of physician under 36, compared to 22.2% of those over 65 (The percentage approval figures for the 36-45-year-old and 46-55-year-old cohorts were 25.7% and 33.3% respectively). This trend was further quantified by van Randwijk, Opsahl [16], who found that "for each additional year of age, physicians were 1.03 times more likely to object to euthanasia (OR=1.03; 95% CI=1.01–1.04)". Terkamo-Moisio, Gastmans [21] describe a similar trend in nurses: "younger nurses agreed more with the active participation [in euthanasia] compared with their older colleagues", which they attribute speculatively to the "more liberal environment in which the younger nurses have grown up". Finally, Pomfret, Mufti [17] showed such a trend extended in students, but in the opposite direction: "Being older, a finalist and a graduate are weakly associated with a greater likelihood of agreeing with such actions". Overall, the finding that being older correlates with less support for MAiD is robust and repeated across a number of countries, specialties, and professions.

IIIc Gender of HCW

Six studies identified the gender of the HCW as a contributing factor to MAiD-opinion divergence. They generally reported the same trend, for example, Randwijk, Opsahl [16] found that women were significantly more likely to object

to euthanasia than men (odds ratio (OR)=2.38; 95% CI=1.56–3.70), which Evenblij, Pasman [12] confirmed with a multivariate analysis. In their study women were less likely to find performing euthanasia conceivable, which was repeated exactly by Brinkman-Stoppelenburg, Evenblij [11]. Piili, Metsänoja [18] confirmed the trend to the contrary, where they found that men were more likely than women to increase the morphine dose to lethal levels upon the request of a terminally ill patient. Women also had divergences of views on specific instantiations of MAiD practices; Schildmann, Junghanss [22] found they were slightly more likely than men to vote for the involvement of "more disciplines and further parties in counselling compared to male respondents (MD: 0.32; CI 0.10-0.53; P ¡ 0.005)".

Evenblij, Pasman [13] found no difference between perceived pressure to grant a MAiD requests in men and women, suggesting that while men and women may have broadly different levels of support for MAiD, this doesn't affect it's prescription when it is legalised.

IIId Psychological factors and outlook of HCW

Five studies investigated the impact of HCWs' psychological patterns on their views and practices of MAiD. Two main themes emerged, namely the HCWs relationships to uncertainty in general, and death specifically. Firstly, Otte, Jung [20]'s study of Swiss physicians concluded that of GPs who avoid talking about PAS, the main reason for not doing so was fear of their own psychological health, due to the uncertainty of their reaction towards it. Schuurmans, Bouwmeester [10] also highlighted feelings such as insecurity, frustration, and anger associated with MAiD consideration, with some of their respondents feeling stressed about technical issues such as "administering the injection correctly, and about the possible legal consequences".

Secondly, Testoni, Bortolotti [23] delineate the impacts of HCWs psychological relationship with death on their opinions of MAiD. They found first a close-to-significant positive correlation with representation of death as annihilation (i.e. not believing in an afterlife or eternal soul etc., where the death of the material body is final and finite) and acceptance of euthanasia. They then link this to HCWs intrinsic and extrinsic religiosity, both of which were significantly negatively correlated with representation of death as annihilation. From this, we can plausibly conclude that religious HCWs are less likely to represent death as annihilation, and are therefore more likely to oppose euthanasia. More specifically G lebocka [24] distinguishes between fear of death and fear of dying. She was unable to correlate fear of dying with more or less conservative views of MAiD legalisation, but suggested that this may not carry over to fear of death, despite their generally strong correlation.

IV Medical factors of patient, IVa Patient's condition

The patient's medical condition(s) was the most studied factor influencing MAiD views among HCWs, with all of the studies demonstrating some form of significant impact. In general, HCWs are generally more supportive of euthanasia for patients dying of physical or somatic illnesses than purely psychiatric ones (Humbeeck, Piers [4], Cleemput and Schoenmakers [15], Verhofstadt,

Audenaert [6], Hodel, Hoff [25]). There was also variability among support for MAiD in different somatic illnesses, which depended on a number of factors:

- Degree of suffering: HCWs are generally more favourable to prescribing MAiD when the patient has a condition that causes them more suffering, which in this study was measured by time expected to suffer (e.g. HCWs agree with MAiD when a patient is expected to have a given amount of pain for a year than for 6 months) and mental versus physical pain (HCWs weighted physical pain as more significant than mental pain) . Verkissen, Houttekier [26], for example, found that conditions of suffering for the patient and their relatives were more consistently met for haematological cancer than other cancers by their oncologist cohort;

- Lack of treatment/inoperability: Most doctors are more willing to prescribe MAiD the less hope of treatment or cure there is. Alminoja, Piili [19] found that GPs were less likely to attempt resuscitation on a patient with an inoperable brain tumour, compared to choosing more supportive palliative care in a comatose patient with prostate cancer, and Thurn, Borasio [27] found that length of prognosis was the only significant factor that affected whether or not a HCW would offer FANH;

- Impact of patient's condition on their capacity: generally, support for MAiD wanes when patients have a condition that tends to limit their capacity, even if they haven't spoken to the patient to gauge this for themselves; Demedts, Roelands [28], for example found that most Belgian nurses supported the idea that patients with severe mental illnesses, including psychotic, resistant depressive, and bipolar disorders are able to make informed euthanasia decisions (83%, 71%, and 70% respectively). They were more sceptical of other psychiatric disorders: just 51% supported the same thesis in the context of dissociative identity disorder.

- Wish to die as a symptom of psychiatric disorder: physicians are generally unwilling to support MAiD when the wish to die it represents is a symptom of a psychiatric disorder. Pronk, Willems et al. (2021b), for example, had a respondent remarking "if someone continues to be suicidal despite you having done everything you can, that distinction [i.e. between suicidality and a lasting wish to die] becomes relevant".

V Psychosocial factors of patient, Va Psychological factors and outlook of patient

A number of studies demonstrated effects of the patient's psychological status or general outlook on the willingness of HCWs to accede to their MAiD requests. Pronk, Willems [29] found that their interviewees differentiated between well-considered/rational wishes to die, and wishes to die as a symptom of mental illness, the latter of which could be impulsive or chronic. Pronk, Sindram [9] found that a number of their physician participants expressed that the psychological nature of some of their patient's suffering was actually less relevant when considering a MAiD request; one participant thought it would be unfair to deny a request on this basis, and thought it should be considered as equivalent to a somatic illness. Other participants, on the other hand, equated psychological suffering with existential suffering, and thus outside the domain of medicine.

In addition, participants of Cleemput and Schoenmakers [15]'s study thought capacity was an essential feature of whether a MAiD request would be accepted. With this standard a number of studies had more repeatable results: Picard, Bier [30] found a majority of physicians would approve of MAiD if the patient was competent to decide thus, even if they had dementia; Cleemput and Schoenmakers [15] found that 62% of physicians thought much the same; Schuurmans, Bouwmeester [10]'s interviewees also concurred. Schuurmans, Crol [31] demonstrated real-life effects of these views on practice: 40 of their 176 GPs had performed euthanasia on patients with dementia, where the majority (37) had been deemed to have capacity to decide so.

Overall, HCWs considered the nature of the suffering and their patient's capacity as influencing their support for MAiD. Psychological suffering generally has two opposite effects on this support, depending on how the clinician views it; on the whole, they either believe that psychological suffering is closer to a psychiatric symptom and thus do not support MAiD for those patients, or they view it as equivalent to somatic suffering and support it.

On capacity, HCWs have a clearer consensus, which is if the patient does not have capacity or is not competent to decide on whether they want MAiD, they are unwilling to prescribe it. This intersects with age; Bolt, Flens [32] found that paediatricians thought it unfair to deny euthanasia if their patient did not have capacity. This might be because, whilst some of their patients under 12 could make, in their opinion, a well-considered euthanasia request, in the majority of cases the parents would make it on their behalf. Most would be willing to reluctantly grant the request in this case; this may be because capacity is conceptualised and assessed differently in children, and their cognitive development (or lack thereof) may mean HCWs have to treat patients differently at the same age (e.g. where one fifteen-year-old may have the wherewithal to make a well-considered end-of-life decision, another may not), or the same patient differently for decision of differing significance (e.g. where a patient's mental state varies over days or weeks).

Vb Age of patient

There was no clear, repeated association between the age of the patient and the HCWs agreeability to MAiD in the reported studies. Significantly, Jahn-Kuch, Domke [5] found that the probability that a HCW approves of MAiD increases along with the age of the patient; they found the corresponding probabilities were 56.8% and 69.5% for patients younger and older than 80, respectively. Evenblij, Pasman [13] also reported significant results, this time regarding the pressure they felt to grant the request: such pressure was felt far greater by those who rejected MAiD requests from patients aged 80 or over, compared to those rejecting requests from patients under 64; 2.03 times greater, to be precise (95% CI 1.08–3.78). Finally, a respondent to [9] provided a potential explanation for why these feelings arose, by explaining that the ending of a young person's life felt "unnatural".

On the other hand, Picard, Bier [30] did not report a significant association between age and the HCWs amenability to MAiD prescription. Evenblij, Pasman [13] reported much the same, suggesting that the differential felt pressure on HCWs, that they also demonstrated varied depending on the

patient's age, does not significantly affect how likely the patient is to actually receive MAiD.

Vc Influence of family/relatives

One of the most significant factors determining the views of HCWs was the influence of the patient's family or relatives. Bergman, Pasman [33] specify a number of difficulties with patient's families, including that they are not ready for their relative to die or have issues with MAiD in general, and exerting pressure on the HCW to influence their decision. Despite only being experienced by 4.5-7.5% of physicians in the study, Cleemput and Schoenmakers [15] explain that relative's pressure may have legal ramifications, as they found that the overwhelming majority of GPs (72%) feared that the influence of relatives was encouraging them to perform MAiD without the express consent of the patient themselves at the decisive moment. Patient's families appear to be more problematic for HCWs when their MAiD request was refused than when it was accepted; Evenblij, Pasman [13] report that physicians were generally more concerned about relative pressure when refusing a MAiD request (28.3% reported this, vs 11.4% who accepted a request), and that of those who refused the request, physicians were far more likely to feel pressured by the family/relatives than the patient themselves (31.7% vs. 6.2% respectively). Both the problems created by family involvement and potential future legal ramifications were linked to burdensome feelings and negative views of MAiD practice overall.

Schuurmans, Crol [31] suggest that these problems of relative pressure can be independent of the disease the patient is suffering from; they found that relative pressure did not significantly differ between patients with or without dementia.

Discussion

This study systematically reviewed 43 articles describing the views of healthcare workers, across multiple specialties and professions, on medical assistance in dying, and some of the factors that have influenced them. Despite the limitations of this study, there are a number of robust findings, based on their repeatability both within this study and in comparison with other literature. Chief among which is that a relative majority of studies found HCWs support the legalization of MAiD. This is consistent with polls of general populations (Ibbetson 2020). Crucial as caveats to HCWs support are significant legal concerns regarding it's application, particularly regarding fear of legal action and the clarity of wording of legislation. Ambiguous terms such as "intolerable suffering" form the greatest sources of concern in this review, which makes intuitive sense, and is of a piece with legislation concerning other ethically ambiguous medical practices; in psychiatry, for example. . .

There are a number of robust findings on the impact of clinical settings on the HCWs tendency to support MAiD. Different specialties have different degrees of support for it, which largely depend on the degree to which they are exposed to it; on the whole, specialties that deal with more dying patients, or who have the capacity to develop long relationships with their patients, tend to support MAiD more, despite longer therapeutic relationships' capacity to negatively impact individual clinician's views. This quantifies the finding that having greater experience with MAiD tends to increase a HCWs support for it in general. However, the

actual practice of MAiD, and the discussions it entails, often negatively affect the HCW-patient relationship, which feeds back into more negative views of MAiD as a whole. Sometimes, however, the HCW can feel empowered by these discussions, and the relationship can be affected positively. Given the findings of this study, these negative views do not seem to be a deal-breaker for HCWs practicing MAiD; they may view the emotional difficulty and negative relationship effects as part and parcel of dealing with death, or they may find some resolution to these negative feelings, leading to the sense of empowerment reported by some studies' cohorts. In any case, most HCWs believe MAiD should be available as a legal option.

In addition to the healthcare setting, there were a number of reliably reported individual factors that influence a HCWs approach to MAiD, and while these can be understood as part of broader social and historical movements, this is outside of the scope of this analysis. Generally, religious HCWs are more likely to be opposed to MAiD practices than their irreligious counterparts. There is limited evidence that this relationship is not fixed over time, and can be influenced by broader cultural factors, and has different effects within different age groups. Secular HCWs can also have irreligious moral codes against MAiD in any case. One explanation for these partly contradictory findings is that fewer and fewer people in Europe identify as religious, thus recent studies in which people do so may be more likely to be devoutly religious, and in turn having more socially conservative beliefs, although this is speculation. Another explanation is that older people tend to be both more religious and, in this analysis, less supportive of MAiD. These findings suggest that the current instantiation of religious attitudes towards MAiD practices is not fixed and is subject, at least in part, to broader social trends, and the second hypothesis suggests there is no causative link at all.

Other individual findings were repeatable, such as the facts that younger physicians and women tend to support MAiD more than their older, male counterparts. Given the concerns already raised about idiosyncratic interpretations of legal criteria for MAiD in countries where it already exists, there is at least scope for MAiD provision to be dependent on the opinion of the HCW responsible for making the decision. More promising however is that the HCWs gender does not seem to affect the rate at which MAiD decisions are approved.

A significant question and problem for healthcare systems is how HCWs categorise the reasons patients give for wanting support ending their life. This analysis does not confirm or deny any specific mechanisms by which HCWs make these decisions, but it does identify some broad questions that can be investigated in further research. Generally speaking, the following characteristics of a patient's illness makes it more likely that they will grant a request for MAiD:

- The condition is principally medical rather than psychiatric - Where the condition is psychiatric, the wish to die is present as long-term, "well-considered", or "rational", as opposed to being a primary symptom of psychiatric disease - It confers an intense, protracted, socially destructive level of suffering - There is no practical scope for treatment, operative capacity, or chance of development of one in the future - The condition retains the decision-making capacity of the patient

- The condition primarily affects older patients, although this point is more contentious and may not be a necessary contingent for all HCWs

Finally, this research indicates a number of practical difficulties experienced by HCWs, which bear significant consideration. There is a substantial evidence base demonstrating the influence of family and relatives of the patient influencing the decision making and practical process of MAiD. While it is difficult to sum up the effects of relative influence as a whole, broadly speaking their involvement tends to increase negative feelings in the HCW. They do this in a number of ways, which tend to cause problems when the wishes of relatives conflict with wishes of the patient or the facilities and services available to them. Sometimes the relatives can have difficulty accepting their loved one wishes to die, and thus attempt to obstruct the process; other times they may support their decision but express frustration at the regulations in place when granting MAiD, which can be directed at the HCW responsible for their loved ones' care. In any case, the dying of a loved one is a traumatic experience that inspires profound grief in everyone involved, a grief that can break down professional roles and boundaries. It is clearly unreasonable to expect anyone to see a loved one die in any circumstance without anger, frustration, and sadness. There is no real scope to eliminate these entirely from this clinical practice. What this review demonstrates is that there are repeatably demonstrated sources of profound negative emotion that are solvable through well-designed legislation and quality healthcare services.

Limitations

There are a number of limitations to this study. Principally, all of the studies are from western Europe, limiting the analysis to countries within the broad socioeconomic paradigms of these countries e.g. no developing countries were included in this analysis. The same applies for factors like religion; in most European countries, Christianity is one of, if not the, dominant religious socio-political structure influencing many people's beliefs around death and end-of-life care. Broader analysis would include other world religions, such as Islam or Hinduism, for comparison.

There are methodological limitations to this study, chief among which are the lack of a standardised framework for analysis of the factors influencing the way healthcare worker's conceptualize and understand ethical issues. This makes it more difficult to compare to existing and future literature. There were also no non-English studies included, which further limits the study cohorts. The lack of a meta-analysis was due in part to the methodology of most studies, but meant that conclusions had to be drawn from the less robust measure of simply whether or not a particular number of studies found a particular factor statistically relevant. This also means the results of this review depend in large part to the publication bias of existing literature, which is difficult to quantify in itself, but certainly conceivable; for example, studies demonstrating that a particular factor is repeatably irrelevant to the views of HCWs would be important for this review but less likely to be included in the available literature.

Conclusion

This review highlights a number of repeatable features of recent literature summarising the views of healthcare workers. Many of the factors were somewhat predictable, as they have demonstrable effects on other ethically contentious healthcare issues; it would be surprising if, for example, religion had no impact on how a HCW views MAiD. Further work should focus on a more nuanced analysis of these factors individually, as in many instances this review only made broad comments. For example, the way the influence of religion seems to change over time in different social circumstances is hinted at but not elaborated here. Many of these factors have implications for the social psychology of healthcare; the research suggesting a relationship between the HCWs views of MAiD, their religiosity, and their conception of death more broadly, requires further explication, as here there was no opportunity to conclusively demonstrate causative links in any direction. There are also broad political implications, as it may be the case that even within a standardised healthcare system, the views and outlook of HCWs responsible for providing MAiD impact it's availability in different areas of a country; this is particularly concerning given the evidence that clinicians can have idiosyncratic views of the same legal terminology.

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Appendix

Appendix 1 PubMed search terms

((doctors) OR (nurses) OR (healthcare practitioners) OR (clinicians) OR (physicians)) AND ((euthanasia) OR (physician assisted suicide) OR (medical assistance in dying))

Appendix 2 Table of included studies and their study cohorts

Authors, year pulished	Country of lead author	Cohort profession(s)	Methodology
Jahn-Kuch et al. 2020	Austria	Physicians	Survey
Van Humbeeck et al. 2021	Belgium	Physicians	Survey
Verkissen et al. 2018	Belgium	Physicians	Survey
Verhofstadt et al. 2020a	Belgium	Physicians	Survey
Verhofstadt et al. 2020b	Belgium	Physicians	Survey
Verhofstadt et al. 2021	Belgium	Physicians	Case Note Review
Demedts et al. 2018	Belgium	Nurse	Survey
Picard et al. 2019	Belgium	Physicians	Survey
Verhofstadt et al. 2022	Belgium	Physicians, nurses	Interview
Schweitser et al. 2020	Belgium	Physicians	Interview
Cleemput & Schoenmakers 2019	Belgium	Physicians	Survey
Van Randwijk et al. 2020	Denmark	Physicians	Survey
Terkamo-Moisio et al. 2019	Finland	Nurse	Survey
Piili et al. 2018	Finland	Physicians	Survey
Alminoja et al. 2019	Finland	Physicians, medical students	Survey
Schildmann et al. 2021	Germany	Physicians	Survey
Thurn et al. 2019	Germany	Physicians	Survey
Kontaxaki et al. 2018	Greece	Physicians	Survey
Malikentzou et al. 2022	Greece	Physicians	Survey
Ntantana et al. 2017	Greece	Physicians, nurses	Survey
Tectonic et al. 2020	Italy	Physicians	Survey
Brinkman-Stoppelenburg et al. 2020	Netherlands	Physicians	Survey
Bergman et al. 2020	Netherlands	Physicians	Survey
De Boer et al. 2019	Netherlands	Physicians	Interview
Pronk et al. 2020	Netherlands	Physicians	Interview
Pronk et al. 2019	Netherlands	Physicians	Interview
Evenblij et al. 2019a	Netherlands	Physicians	Survey
Pronk et al. 2021	Netherlands	Physicians	Survey, Interview
Schuurmans et al. 2021	Netherlands	Physicians	Survey
Evenblij et al. 2019b	Netherlands	Physicians	Survey
Schuurmans et al. 2019	Netherlands	Physicians	Interview
Ten Cate et al. 2017	Netherlands	Physicians	Interview
Bolt et al. 2017	Netherlands	Physicians	Survey
Evenblij et al. 2019c	Netherlands	Physicians	Survey
Schuurmans et al. 2020	Netherlands	Physicians	Survey
Głębocka 2018	Poland	Nurse	Survey
Sousa et al. 2022	Portugal	Medical students	Survey
Lynøe et al. 2021	Sweden	Physicians	Survey
Otte et al. 2017	Switzerland	Physicians	Focus Groups, Interview
Gamondi et al. 2017	Switzerland	Physicians	Interview
Hodel et al. 2019	Switzerland	Physicians	Survey
Clayton & Nabhani-Gebara 2021	UK	Pharmacy students	Survey
Pomfret et al. 2018	UK	Medical students	Survey

Appendix 3. Breakdown of factors into studies that found it significant or insignificant

Factor category	Factor	Articles finding this factor significant	Articles finding this factor insignificant
HCW-centred (professional)	Specialty of HCW	Jahn-Kuch et al. 2020 van Humbeeck et al. 2021 Piili et al. 2018 Schildmann et al. 2021 Kontaxaki et al. 2018 Bergman et al. 2020 Pronk et al. 2021 Evenblij et al. 2019b Evenblij et al. 2019c Lynøe et al. 2021	Picard et al. 2019
	Prior engagement of HCW w/ MAiD	Verhofstadt et al. 2020b Schildmann et al. 2021 Ntantana et al. 2017 Brinkman-Stoppelenburg et al. 2020 Evenblij et al. 2019a Evenblij et al. 2019b Evenblij et al. 2019c	Picard et al. 2019
	Awareness/security of legal status of HCW	van Humbeeck et al. 2021 Verhofstadt et al. 2020b Picard et al. 2019 Verhofstadt et al. 2022 Ntantana et al. 2017 Testoni et al. 2020 Bergman et al. 2020 de Boer et al. 2019 Pronk et al. 2019 Schuurmans et al. 2019 ten Cate et al. 2017 Evenblij et al. 2019c Schuurmans et al. 2020	Lynøe et al. 2021
	HCW -patient relationship	Verhofstadt et al. 2020a Verhofstadt et al. 2020b Verhofstadt et al. 2022 de Boer et al. 2019 Pronk et al. 2019 Pronk et al. 2021 Schuurmans et al. 2019 Otte et al. 2017	
HCW-centred (personal)	Psychological factors of HCW	Testoni et al. 2020 Schuurmans et al. 2019 Evenblij et al. 2019c Głębocka 2018 Otte et al. 2017	
	Gender of HCW	van Randwijk et al. 2020 Piili et al. 2018 Schildmann et al. 2021 Brinkman-Stoppelenburg et al. 2020 Evenblij et al. 2019b Sousa et al. 2022	Picard et al. 2019 Evenblij et al. 2019c
	Religiosity of HCW	Cleemput & Schoenmakers 2019 van Randwijk et al. 2020 Terkamo-Moisio et al. 2019 Piili et al. 2018 Alminoja et al. 2019 Schildmann et al. 2021 Testoni et al. 2020 Brinkman-Stoppelenburg et al. 2020 Evenblij et al. 2019b Sousa et al. 2022 Thurn et al. 2019 Otte et al. 2017 Clayton & Nabhani-Gebara 2021 Pomfret et al. 2018	Jahn-Kuch et al. 2020 van Randwijk et al. 2020[sic] Evenblij et al. 2019c
	Age of HCW	Jahn-Kuch et al. 2020 van Randwijk et al. 2020 Terkamo-Moisio et al. 2019 Piili et al. 2018 Evenblij et al. 2019b Evenblij et al. 2019c Lynøe et al. 2021 Gamondi et al. 2017 Pomfret et al. 2018	Picard et al. 2019 Evenblij et al. 2019c Hodel et al. 2019
Patient-centred (medical)	Patient's condition/disease	van Humbeeck et al. 2021 Verkissen et al. 2018 Verhofstadt et al. 2020a Verhofstadt et al. 2020b Demedts et al. 2018 Picard et al. 2019 Cleemput & Schoenmakers 2019 Alminoja et al. 2019 Bergman et al. 2020 Pronk et al. 2020 Pronk et al. 2019 Evenblij et al. 2019a Pronk et al. 2021 Schuurmans et al. 2019 Bolt et al. 2017 Evenblij et al. 2019c Schuurmans et al. 2020 Sousa et al. 2022 Thurn et al. 2019 Hodel et al. 2019 Clayton & Nabhani-Gebara 2021	
Patient-centred (personal/ psychosocial)	Age of patient	Jahn-Kuch et al. 2020 Bergman et al. 2020 Evenblij et al. 2019a Pronk et al. 2021 Bolt et al. 2017 Evenblij et al. 2019c Sousa et al. 2022 Clayton & Nabhani-Gebara 2021	
	Psychological factors of patient (inc. competence/ capacity)	Pronk et al. 2020 Pronk et al. 2021 Picard et al. 2019 Cleemput & Schoenmakers 2019 Schildmann et al. 2021 Schuurmans et al. 2019 Bolt et al. 2017 Schuurmans et al. 2020 Clayton & Nabhani-Gebara 2021	

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RESEARCH

The Cognitive Model of Depression: A Retrospective and Prospective View of Its Evolutionary Journey

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Abstract

This review examines the cognitive theory of depression proposed by Aaron Beck and evaluates its relevance and applicability in contemporary psychological research. Depression is a significant public health concern that can lead to severe impairment in social, occupational, and academic functioning, making it an important topic of study for researchers and healthcare professionals alike. The study analyses the fundamental aspects of Beck's cognitive model from a psychological point of view, the evolution of his cognitive theory as a model of depression, and the strengths and limitations of Beck's cognitive theory. The aim of the review is to provide a critical analysis of the cognitive theory and its contribution to the understanding and treatment of depression.

Introduction

Depression is a complex mental disorder that is characterized by a persistent feeling of sadness, loss of interest, and a lack of pleasure in daily activities. It is a significant public health concern that can lead to severe impairment in social, occupational, and academic functioning. The impact of depression on individuals and society is substantial, making it an important topic of study for researchers and healthcare professionals alike. In this systematic review, we will examine the cognitive theory of depression proposed by Aaron Beck and critically evaluate its relevance

and applicability in contemporary psychological research. The aim of this study is to analyse the cognitive theory of depression proposed by Beck which has been widely regarded as a essential contribution to the understanding and treatment of depression. This study has been divided into two main parts to analyse the fundamental aspect of the proposed topic and critically evaluate the pioneering work held by Aaron Beck in order to provide a critical analysis of the cognitive theory. Therefore, this study begins by providing an overview of the principles of Beck's cognitive model from a psychological point of view. Following that, the evolution of Beck's cognitive theory as a model of depression is stipulated to examine the core aspects of his cognitive theory and its progressive development in the course of time. Finally, strengths and limitations of Beck's cognitive theory are discussed in order to gain a more comprehensive understanding of the theory.

Keywords: cognitive triad, schema, negative thoughts, cognitive distortions and biases, dysfunctional beliefs

Principles of Beck's Cognitive Theory

This section provides an overview of the fundamental concepts and assumptions that underpin Beck's Cognitive Theory. It explores how Beck's model conceptualizes the interaction between thoughts, emotions, and behaviour, and how it identifies specific cognitive patterns and processes that contribute to the development and maintenance of depression. The section discusses key concepts such as schema, cognitive restructuring, and metacognition, and how they are used to identify and modify negative thought patterns. It also highlights the importance of empirical research in supporting the development and refinement of Beck's cognitive model.

The core foundation of cognitive theory of psychopathology and cognitive treatment of various psychiatric diseases was established more than 50 years ago. Since then, there has also been consistent progress in the development of cognitive theory and therapy, along with their empirical testing(Beck, 2005). On the basis of empirical evidence, it can be posited that Beck's cognitive model has given an evidence-oriented approach for conceptualising and treating psychiatric problems. (Beck Haigh, 2014). The creation of therapeutic techniques has always been transcended by constructing a coherent conceptual framework. Beck's original focus was on depression since the field available to conduct clinical research on his testable hypothesis was open (Beck, 2008). His research technique embraced the subsequent stages; finding unique cognitive aspects from clinical data generated from diverse illnesses, developing and testing measures to codify these findings, and formulating therapeutic guidelines by fulfilling the following aims: developing a complete theory of psychopathology aligned well with the psychotherapeutic method, investigating empirical evidence for the theory and conducting empirical research that examined the utility of the therapy(Beck, 1963a).

The rationale of his theory is based on a model that encompasses thoughts, antecedent events and feelings. This model identifies negative cognitive content as a critical component of depressive symptomatology. Additionally, a large

number of individuals have recurring, persistent, and uncontrollable negative automatic thoughts that arise spontaneously and rapidly and are an immediate interpretation of any given scenario as a response to the above-mentioned events (Beck, 1976). In the light of these findings, Beck posed the question: "Why are the negative thoughts occurring?" Based upon the clinical observations supported by research, patients had highly charged dysfunctional attitudes or beliefs called schemas about themselves, their world, and future named a cognitive triad (Beck, 1963a). These schemas, also called core beliefs and used interchangeably by many authors, are characterised by cognitive distortions, such as personalisation, selective abstraction, which are negatively biased errors in thinking that are amount to increased vulnerability to depression (Dozois Beck, 2008). Schemas are formed early in a person's development and operate as "filters" through which current knowledge and experience are processed(Knapp Beck, 2008). As schemas are triggered by a particular event or series of events, they skew the system of processing information, causing it to translate specific experiences into distorted negative interpretations(Beck, 2008) from the early stages of perception through working memory, interpretation, recall, and long-term memory(Beck, 2002).

Beck's cognitive model is primarily a theoretical framework rather than a therapeutic model, although it is often integrated into cognitive therapy (CT) or cognitive-behavioural therapy (CBT) due to its foundational role in the development of CBT. In the early 1960s, a "cognitive revolution" began to emerge(Knapp Beck, 2008). For over 50 years, Beck's cognitive model has provided an evidence-based way to conceptualise and treat psychological disorders (Beck Haigh, 2014). The first cognitive approach to psychopathology was founded on an information-processing model and initially developed to describe the psychological processes involved in depression. A number of researchers have examined the cognitive model of depression since it was first proposed in 1967 (Beck, 1967). A 1985 evaluation of 180 papers that included 220 investigations of this model found that 91 per cent of the research findings supported the model, whereas 9 per cent were either non-supportive or conflicting(Hollon, Kendall, Lumry, 1986). Beck notes that his own experiences with psychoanalytic therapy shaped the evolution of cognitive therapeutic investigations. As reported by the recent analysis of Beck and Haigh, the revised theoretical model provides a framework for referring to significant problems about the phenomenology of disorders that were not addressed in prior revisions of the original model(Beck Haigh, 2014). Unequivocally, drawing upon the fact that psychological issues were examined from the point of view of cognitive distortions in depression (Beck, 1963), Beck then established the paradigm of modes, which express a complex formulation of schemas pertinent to expectancies, self-evaluations, rules, and memories in the further refinement of the model (Beck, 1996). Identifying the new additions to the theory, continuity of an adaptive and maladaptive function, dual information processing, schema energising, and attentional focus have been added to the theory. The central hypothesis of Beck's cognitive model has been the principle that certain beliefs are associated with a concept of cognitive vulnerability, which is the so-called 'stress-diathesis model'. For instance, if a person holds the cognitive vulnerability

to patterns of loss and failure, the emotional and behavioural outcomes would include grief, hopelessness, social withdrawal and rumination, as observed in depression (Knapp Beck, 2008). Beck's model of vulnerability to depression was modified, implying that predisposing beliefs may be differentiated based on the patient's personality (Clark, Beck, Brown, 1992). Another crucial aspect of the evaluation of cognitive model created by Beck is that the proposed role of biased schemas, which are essential components of the generic cognitive model, should be interpreted in the field of genetic influences, neurobiological, and environmental models of psychopathology(Beck Haigh, 2014).

The Evolution of Beck's Cognitive Theory of Depression

Within regard to the review of Beck's cognitive model, there must be due consideration to give weight on the progressive development of this theory in the course of time. Aaron Beck's cognitive theory of depression has undergone significant development since its inception in the 1960s. Initially, Beck proposed that depression was the result of a negative cognitive triad, which included negative beliefs about the self, the world, and the future. These negative beliefs were thought to create a negative schema that would lead to negative automatic thoughts and ultimately, to depressive symptoms(Beck, 2002). Over time, Beck's cognitive theory has evolved to incorporate more nuanced and sophisticated understandings of the cognitive processes involved in depression. For example, Beck and his colleagues identified a number of cognitive distortions that were commonly observed in depressed individuals, such as arbitrary inference, selective abstraction, and overgeneralization. These cognitive distortions were thought to contribute to the development and maintenance of depressive symptoms. More recently, Beck's cognitive theory has been expanded to include a focus on metacognition or thinking about thinking. This new approach emphasizes the importance of understanding how individuals think about their thoughts and emotions, rather than just focusing on the content of those thoughts and emotions. This has led to the development of metacognitive therapy, which aims to address maladaptive thinking processes that contribute to depression and other mental health disorders(Eichbaum, 2014).

Having discussed the evaluation of Beck's cognitive theory over time, it should be vital to differentiate the model from other theories, tools and therapies as a cognitive model of depression in the light of modern evidence in relation to other proposed models. It should not be forgotten that Beck formulated a cogent theoretical framework before therapeutic strategies evolved. The publications of George Kelly, particularly his construct theory, had a significant impact(Knapp Beck, 2008). When combined with Piaget's notion of schemata (Piaget, 1954), it led to Beck's equivalent description of schemas (Knapp Beck, 2008). Beck's theory is considered to be a 'clinical-empirical' model and has been interpreted into cognitive therapies. In spite of this, it appears that the Beck's cognitive method has run into difficulties. To overcome these shortcomings, a wide array of cognitive theories has been developed over time considering the modern evidence. For instance, within the associative network theory of mood and

memory created by Bower provides a framework to understand the cognition-emotion relationship (Bower, 1981). The hypothesis states that when we are going through a particular mood, there is high possibility to recall events that were previously connected with that emotion which means that the memories and concepts associated with negative emotions are reactivated. To put it another way, in depressed moods, the inclination to access this form of cognition may be a significant element of cognitive vulnerability to depression(Teasdale, 1993). Another alternative science-driven model that overcomes the shortcomings of Bower's associative network theory and Beck's cognitive model is 'The Interacting Cognitive Subsystems (ICS)' framework shaped by Barnard and Teasdale(Barnard Teasdale, 1991). As reported by Teasdale, how we approach therapy today and how we develop new treatment approaches in the future are highly affected by this ICS framework(Barnard Teasdale, 1991). To exemplify how depressive thinking works in this framework is that depression is maintained through the regeneration of depression-related implicational schematic models, which provide distorted lower-level meanings in the form of negative appraisals, attributions, and instructions to access negative information in memory, leading to negative, depressed thinking. Furthermore, negative automatic thoughts, negative visual pictures, and particular negative meanings are not actual antecedents to depression and have no direct influence on depression (Teasdale, 1993). However, another cognitive theory to comprehend depression asserts that depression occurs as a result of hopeless attempts to escape a "negative" circumstance which is the so-called 'learned helplessness' theory created by Seligman (Seligman, 1974). Despite the fact that Seligman's theory can explain depression to some extent, it neglects to account for cognitions (thoughts) that have been reconsidered and reformulated by Abramson, Seligman, and Teasdale, consequently with a cognitive version of this theory (Abramson, Seligman Teasdale,1978).

This notion has been the impetus for a true explosion of study in the field of cognitive susceptibility to depression, which has served as a catalyst for the explosion. The vast majority of today's cognitive theories of depression have been built on top of this fundamental diathesis–stress framework, which has been subjected to a number of revisions and expansions(Dozois Beck, 2008). Ingram (2003) proposed a cognitive taxonomy so that researchers could more consistently operationalize and evaluate different constructs of cognition related to depression. This was done so that the taxonomy could be used to categorise different types of information. The cognitive structures, propositions, operations, and products are the four primary components of the cognitive taxonomy that were developed. The term "cognitive structure" refers to the internal representation and organising of information that is stored in memory. Cognitive structure, along with cognitive premises (such as fundamental beliefs), is what makes up the schema. The processes of the schema are referred to as cognitive operations, and some of the variables involved in cognitive operations include attention, encoding, retrieval, and interpretation. In conclusion, cognitive products are the thoughts and beliefs that are easily accessible and are the result of the interaction between schemas and the processing of information(Dozois Beck, 2008).

Yet, despite the fact that Beck's model shows

that the first development of maladaptive schemas, beliefs, and assumptions happens in early childhood (Beck, 1963), this concept has not been fully described or examined until very recently (Rose Abramson, 1992). There has been a lot of study done on maladaptive cognition and schematic processing, but not a lot of research on how core beliefs associated to depression develop in the first place. This is in contrast to the amount of research that has been done on these topics(Dozois Beck, 2008).

Conclusion

Taking the aforementioned points into consideration, it can be concluded that a number of systematic theories in relation to the cognitive aspect of depression have been postulated by the pioneers; however, there is no doubt that Beck's cognitive model represents a fundamental evidence-based approach to apprehend the general understanding of the cognitive aspect of emotional disorders arising from depression which has been the major subject of the model. To fulfil the aim of this study, it must be pointed out that through profound contributions of Beck and others enhanced the cognitive approaches, there has been constant improvement in the development of cognitive theory and therapy for more than 50 years, and this evaluation has enabled the progressive development of the model and of the psychotherapy acquired from it (Beck, 1976). Correspondingly, Beck's theory has been improved and expanded upon over the course of time. Yet, the core assumptions of cognitive theory of depression have, for the most part, been well supported by the research that has been conducted(Dozois Beck, 2008). One strength of Beck's cognitive theory of depression is its evidence-based approach. The theory has been extensively researched and has been shown to be effective in understanding and treating depression (Beck, 1967). This provides a solid foundation for its use in clinical practice. However, despite the strengths of Beck's cognitive theory, there are also several limitations that need to be considered in order to gain a more complete understanding of the theory. For instance, despite its focus on individual cognitive processes, the theory may overlook the impact of social and cultural factors on depression, which can be significant factors in the development and maintenance of the disorder. Additionally, the theory's focus on negative thoughts and beliefs as the primary cause of depression may oversimplify the complexity of the disorder. Depression is a multifaceted condition that may have multiple underlying causes, and an overemphasis on cognitive factors may overlook other potential causes and contributing factors. However, it should be noted that Beck's cognitive theory of depression provides a beneficial structure for comprehending the influence of thoughts on our psychological well-being. It has influenced the development of therapeutic interventions and has added to our perception of the significance of cognition in the context of depression.

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RESEARCH

The 13-year Trek: Completion for Genomics and Momentum for Connectomics

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Abstract

The Human Genome Project (HGP) and the Human Connectome Project (HCP) are two landmark scientific research projects aimed at unlocking the secrets of human biology. While the HGP successfully mapped the entire human DNA sequence in 2013 after 13 years of international collaboration, the HCP, launched in 2010 under the Blueprint Grand Challenge, will reach the same 13-year benchmark in 2023. During the same timeframe, connectomics still faces substantial challenges in achieving completion due to the complexity of mapping neural connectivity. This review adopts a retrospective approach to document how methodological innovations during pilot studies led to acceleration in both genomics and connectomics. Particular attention is given to discussing roadblocks of connectomics research, which contributed to comparatively slower progress than the HGP.

Introduction

The Human Genome Project

The Human Genome Project (HGP) was a seminal international research endeavour aiming to map and sequence the entire human genome. This ambitious undertaking involved locating approximately 100,000 human genes and approximately three billion base pairs. HGP was launched in April of 1990 under the joint project of the U.S. Department of Energy (DOE) and the National Institutes of Health (NIH) (Green et al., 2015).

The HGP set out a five-year plan (1991-

1995) for the forecasted 15-year research effort, which aimed to refine sequencing and analytic technologies for mapping the human genome. Specific goals and respective rationales were established in various areas, including mapping the human genome and model organism genomes, data collection and distribution, ethical, legal, and social considerations, research training, technology development, and technology transfer ("The U.S. HGP: The First Five Years," 1990).

Over the course of thirteen years, the HGP brought together twenty different universities and research centers across the United States, United Kingdom, France, Germany, Japan, and China ("HGP Fact Sheet," 2022). Through this collaborative research effort, the HGP pioneered a series of genetics laboratory techniques, data analysis models, and the research mode of consortium-based projects. In 2013, the project was officially announced to be completed. It is widely considered a flagship venture that paved the way for further research in fields such as personalized medicine, forensic science, agriculture, genome editing, and more ("15 Ways," 2019).

The Human Connectome Project

A connectome is a comprehensive map of the spatiotemporal location of individual neurons and synaptic connections in the brain. The Human Connectome Project (HCP) was launched in 2010 with the ambitious goal of mapping the entire human brain, including its structural and functional connectivity (Van Essen et al., 2012). The project generated significant interest and discussions within the neuroscience community and is considered one of the most challenging undertakings of the 21st century.

In September 2010, the National Institutes of Health (NIH) awarded $40 million to two consortia as part of the Blueprint Grand Challenge under the NIH Blueprint for Neuroscientific Research framework ("$40 Million Awarded to Trace Human Brain's Connections," 2015). The first consortium, the WU-Minn-Ox consortium, was centred at the University of Washington, the University of Minnesota, and Oxford University. The second consortium, the Harvard-MGH-UCLA consortium, was centred at Harvard University, Massachusetts General Hospital, and the University of California Los Angeles (Van Essen et al., 2013).

As of 2023, the HCP has been underway for 13 years, marking a similar timeframe as the HGP. While the HGP successfully celebrated its completion after 13 years, brain mapping is still considered a grand challenge in science, raising questions regarding the HCP's current progress and prospective completion. This review provides an overview of innovative methodologies developed in the HGP and HCP pilot studies. Furthermore, this review evaluates the complexities of connectomics in terms of scale, variability, and neuroplasticity, which may explain the slower progress of the HCP.

Methodologies of the Pilot Studies: HGP and HCP-YA

HGP Pilot Studies

The establishment of the HGP in 1990 was largely based on six pilot studies launched in April of 1996 by the National Human Genome Research Institute (NHGRI), which accounted

for the feasibility of large-scale rapid genome sequencing. ("Pilot Study," 2010). The NHGRI identified the following six principal investigators that worked on individual projects which culminated the complete methodology of HGP ("Pilot Study," 2010): (1) Mark D. Adams, The Institute for Genomic Research, Rockville, MD; (2) Richard A. Gibbs, Baylor College of Medicine, Houston, TX; (3) Eric S. Lander, Whitehead Institute for Biomedical Research, Cambridge, MA; (4) Richard M. Myers, Stanford University, Stanford, CA; (5) Maynard V. Olson, University of Washington, Seattle, WA; (6) Robert H. Waterston, Washington University, St. Louis, MO.

The six pilot studies achieved a series of the following methodological advances. (1) Adams et al. (1991) translated efficient sequencing protocols in microbial DNA to sequence human DNA fragments by using complementary DNA (cDNA) to generate expressed sequence tags, which are then assigned to chromosomes to amplify DNA fragments. In addition to sequencing small human DNA fragments in large quantities, this study also effectively established DNA libraries and software to pursue automation in sample matching and data assembly. (2) Dr. Gibbs's group at the Baylor College of Medicine utilized precise DNA purification and reaction chemistry method to develop new fluorescent dyes for accurate readings of DNA bases. (3) Lander et al. (2001) developed a high-throughput automated mapping machine. They sequenced the genome of several individuals and compared their sequences to identify single nucleotide polymorphisms (SNPs) and other genetic variations. (4) Myers' group developed a mapping methodology that required less computing power for more up-front mapping. (5) The Olson group effectively reduced the number of sequencing reactions required by lending from the random-clone strategy for genetic restriction mapping in yeast (Olson et al., 1986). (6) The Waterson group aimed at modelling genomes of model organisms like Caenorhabditis elegans and mice, with the aim of rapidly releasing data to the public.

Human Connectome Project Young Adult (HCP-YA)

The HCP-YA study underwent two phases of research over five years. Phase I (Fall 2010 – Spring 2012) optimized data acquisition hardware, pulse sequencing, and magnetic resonance (MR) pre-processing protocol. Phase II (Summer 2012 – Fall 2015) acquired and analyzed neuroimaging and behavioral data from 1,200 healthy adults aged 22-35, taken from around 300 families of twins and their non-twin siblings ("HCP Young Adult," n.d.).

In the HCP-YA study, all subjects were scanned on customized 3T Siemens Skyra scanners at the University of Washington (Uğurbil et al., 2013). In addition, a subset of 184 subjects was scanned on 7T scanners at the University of Minnesota, and a smaller subset of 95 subjects was scanned on combined MEG and EEG scanners at St. Louis University (Wu et al., 2019). Standard Siemens 3T Skyra scanners function at 40 mT/m gradient amplitudes. However, by installing Siemens SC72 gradient coil and gradient power amplifiers, the customized 3T scanners increased gradient strength to 100 mT/m (Van Essen et al., 2012). This upgrade provided a higher signal-to-noise ratio, allowing for better image resolution and contrast, leading to a more accurate mapping of

brain connectivity (Elam et al., 2021).

Nevertheless, the increased gradient strength also results in larger gradient distortions, affecting image quality and accuracy ("MR Pre-processing," n.d.). Therefore, a specialized pulse sequencing method and pre-processing pipeline were developed to correct these distortions. The pulse sequencing technique used in the HCP-YA study was an optimized multiband (MB) pulse sequence (Setsompop et al., 2011). This technique is an accelerated imaging approach that enables the acquisition of multiple brain slices simultaneously, which increases data acquisition efficiency and reduces image distortion caused by head motion. In addition, the refined pre-processing pipeline included several steps, such as gradient non-linearity correction, motion correction, and distortion correction (Sotiropoulos et al., 2013). The distortion correction step used a hybrid method combining both field map-based and image-based distortion correction techniques. This method corrected for susceptibility-induced distortion, eddy current-induced distortion, and head motion-induced distortion (Sotiropoulos et al., 2013).

Results

Human Genome Project Pilot Studies

The pilot projects conducted during the Human Genome Project (HGP) were instrumental in culminating the final sequencing strategies for the human genome. According to Landers et al., the pilot studies successfully mapped 15

Notably, the pilot studies pioneered the use of whole genome shotgun sequencing, which was later widely implemented in the actual HGP. These studies demonstrated the feasibility of large-scale accurate genome sequencing. They encouraged maximization of data release, leaving shorter intervals between generation and public release of data compared to usual bioscience results.

Adopting the Bermuda Principles in 1996 further accelerated the data-sharing policy in the genomics field, as it set out clear regulations for the public release of genetic data. These principles agreed to genomics data being released into the public database within 24 hours of generation. As a side outcome of extensive databases for publicly accessible data, this fostered higher processing power platforms that encouraged the implementation of cloud computing in genomics.

Human Connectome Project Young Adults

The pipeline developed specifically for the HCP-YA study has been widely adopted in subsequent HCP studies, as it has been shown to improve the accuracy and reliability of connectome mapping (Glasser et al., 2016). With the improvements in scanners, three modalities benefit from higher acquisition rates and less loss of signal-to-noise ratio (SNR). The modalities in HCP-YA included diffusion MRI (dMRI)/tractography, resting-state functional MRI (r-fMRI), and task-fMRI (t-fMRI). Products of mapping structural connectivity include T1-weighted (T1w) and T2-weighted (T2w) structural images that display myelin content in the cerebral cortex and cortical thickness (Glasser et al., 2016). For functional connectivity maps, t-fMRI protocols performed under task-based conditions demonstrate local neural activity as a response to functional

activations (Glasser et al., 2016).

In addition to its methodological advancements, the HCP-YA study was also notable for its data sharing initiatives. The release of raw and processed data at different levels, as well as the sharing of structural and functional connectivity maps, represented a departure from traditional scientific publication practices. The Connectome Coordination Facility (CCF), a central anchor that documents ongoing and completed connectome projects under the NIH Neuroscience Blueprint, is another significant accomplishment of the HCP. The CCF also includes the Connectome Workbench and the Connectome Database (ConnectomeDB), which are both open-access informatics tools. The Connectome Workbench is a graphic tool that enables flexible visualization of brain surfaces and cortical volumes. This tool allows drawing and annotation. ConnectomeDB provides free and efficient access to unprocessed or minimally processed neuroimaging data. These data contain quantitative data of subjects as well as scanned images.

In summary, the HCP-YA study was a significant milestone in connectomics research, and its innovative methods have contributed to the development of advanced neuroimaging techniques and pre-processing pipelines. The use of customized 3T and 7T scanners, along with the specialized pre-processing pipeline and MB pulse sequencing technique, allowed for the acquisition of high-quality, high-resolution data, leading to a more comprehensive understanding of brain connectivity. These methodological advancements have paved the way for subsequent HCP studies and other large-scale connectomics research projects.

Discussion

As seen, the HGP and the HCP bear a striking resemblance in their collaborative and pioneering approach toward large-scale data acquisition and processing. The pilot studies conducted by both projects served as a means of validating the feasibility of their respective endeavours. However, this raises concerns regarding the prospective completion date for the HCP, given a much slower progress under the same timeframe. Essentially, major roadblocks of connectomics research can be categorized into substantial scale, immense participant variability, and neuroplasticity. As a result, these complications have resulted in a protracted timeline for the Connectomics initiative.

The first major limitation of current connectome research is limitations in scale. The original HCP-YA study investigates neuronal connections on a macroscopic level, which highlights long-distance connections between large grey matter regions of the brain with MRI voxels of approximately 1-2 mm, in vivo (Van Essen et al., 2012). This approach is feasible in human and mammalian brain imaging. In essence, macroscopic connectomes, although of significantly lower resolution than microscopic connectomes with voxels less than 1 mm, require lower processing power and contain less data storage. Currently, microscopic connectomes at the level of individual neurons can only be performed in mice and other animal models. To illustrate, a single cubic millimeter of the human brain's cerebral cortex tissue in the temporal brain culminated in a data volume of approximately

1.4 petabytes (Amunts Lippert, 2021; Shapson-Coe et al., 2021). Thus, the technical barriers in storage technology and data processing are inevitable backend obstacles that extend outside the scope of biosciences.

Secondly, inter-individual variability heavily complicates brain mapping. HCP-YA attempts to tackle this issue via sample selection of monozygotic and dizygotic twins to account for factors in gene expression and socioeconomic background (Van Essen et al., 2012). Variable features in macroscopic neural structure may include cortical folding, total brain mass, cortical thickness, grey and white matter density, and more. Furthermore, in the microscopic perspective, neural structure amongst different individuals may also differ in features like brain density, spatial placements and length of neurite endings, and branching patterns (Sporns, 2013). In addition, functional connectivity also displays significant disparity amongst different individuals based on experience and task-based neural development. That is, a difference in performance level at completing a specific task contributes to diverse functional connectivity maps (Sporns, 2013).

Finally, an individual undergoes drastic reformation of neural connections throughout their life as a response to a multitude of factors involving genetic expression, diet and exercises, episodic experiences, emotional traumas, language acquisition, and more. For example, Draganski et al. (2004) showcased the malleability of the brain via task-based learning. Subjects were asked to learn juggling for three months and cease juggling for three months after mastering it. MR scans were taken before and after learning how to juggle, and the third and final scan took place after three months of not practicing. Voxel-based morphometry enabled visualization and analysis of white and grey matter change. The results display a significant increase in grey matter in the mid-temporal area and the left posterior intraparietal sulcus after learning how to juggle, which then decreased upon not practicing. This suggests a high level of neuroplasticity, by which structural synaptic connections are temporary and affected by active training-dependent rehearsal. There is vast potential in exploring the structural variability in connectome research, which is likely to be addressed in developmental connectome projects.

Conclusion

The Human Connectome Project (HCP) and the Human Genome Project (HGP) share a common approach to validating the feasibility of large-scale data processing through pilot studies. However, the differences in progress between the two projects highlight the underlying challenges in connectomics research. The brain is a dynamic and complex organ, and its structural connections vary with age, mental disorders, substance abuse, and other physiological deficits. As highlighted by Dr. Richard A. Gibbs, the principal investigator of one of the HGP pilot studies in his 2020 commentary, "necessity speeds invention" (Gibbs, 2020). In the same respect, the rapid growth in connectomics research has created a demand for supercomputers with processing power to accommodate the database.

Despite the challenges, the progress made in the HCP has ushered in a new era of understanding the brain's structure, function, aging process, and diseases. The

accomplishments in connectomics research extend beyond technological advancements in hardware and parcellation methods. The open accessibility of thousands of raw and processed datasets has fostered growth within the neuroimaging community.

In conclusion, methodological advancements in pilot studies effectively propelled breakthroughs in both genomics and connectomics. The elongated timeline of connectomics research highlights its complexity and non-linear approach to research. Given the above, after 13 years, it remains a young scientific field and continues to gain momentum.

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Neurosphere Student Journal
King's College London Neuroscience Society

PERSPECTIVES

The State of Undergraduate Research Training

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As I reflect on the past three years of the Neurosphere Journal, I'm reminded of an e-mail exchange I had with the senior tutor for neuroscience at King's College London: I had just concluded my studies in neuroscience and been sent the customary end-of-year feedback form by the department. As an individual with too many thoughts that I can drone on about, I instead emailed a 1000 word opinion piece lamenting the lack of research skills I had learnt over the preceding three years, and questioned if university education should be to teach nice and interesting topics, or to train the next generation of scientists.

Indeed, undergraduate participation in research is paramount in inspiring and training the next generation of scientists and clinician-scientists (Adebisi, 2022). Current undergraduate research training programmes tend to focus on generalised concepts of experimental design, with practical exposure to traditional laboratory skills using guided exercises with known outcomes – a pedagogical approach with dubious benefits to students (Beheshtian et al,. 2023). However, with the scientific literature base growing at an exponential rate (Bronmann et al., 2021), it has never been more important to teach students the necessary skills to discern high-powered, high-impact research from the sea of mass-produced redundant, misleading, or conflicted research (Ioannidis, 2005, 2016). It was with these ideas in mind, and a fortuitous vacancy for an Editor-in-Chief at King's College London Neuroscience Society, that I founded the Neurosphere Student Journal.

Our core activities at Neurosphere differ from those at a traditional journal. Rather than publishing previous drafted manuscripts, we provide a free, near-peer opportunity for early-years students to collaboratively learn how to critically analyse papers through with peer reviewing, and how to conduct a literature search that results in a systematic review. In our inaugural year of 2020-21, we worked exclusively within the walls of King's College London for membership of the Neuroscience Society, and solidified our journal format by the third edition. Our second

year of operation saw Samah Sabreen taking the helm as Editor-in-Chief, with myself assuming the role of Chairman to guide the Journal's long-term growth. It was this 2021-22 season that saw us expanding to become a pan-London enterprise, with authorship from King's College London, University College London, and Imperial College London. This year, with Alex Ephstein as Editor-in-Chief, we've mentored 48 science and medical students from across the United Kingdom and have cumulatively published 40 pieces of research with an expanded 20-strong international team of editors and peer reviewers! Next year will mark a new era for the journal, as we formally secede from King's College London Neuroscience Society. Whilst we undoubtedly will retain a special relationship with the College and its students, we do so for two main reasons:

1. Over the years our editorial and peer review team has grown into a 20-strong membership, a number that now outnumbers the society committee itself. By becoming independent, we can better focus our resources on the journal itself.

2. By being a constituent of King's College London Neuroscience Society, our core leadership all stem from King's College London Student Union elections. By seceding from the Neuroscience Society, we open the door for future students to join and lead from other institutions.

Although we will no longer carry the King's College London Neuroscience Society name, we will continue to provide the crucial step between university education and academia. We have some brand new plans for next year, and on behalf of Neurosphere, hope you are just as excited as we are for the future!

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ABOUT US

Our Neuroscience Society

King's College London Neuroscience Society was founded in 2005 with the aim of uniting the College's subject-impassioned students; by encouraging discussion, dissemination of ideas, and engagement of students with neuroscience and its allied disciplines, our goal is to provide a platform for student inspiration, scientific development, and the pursuit of original research to advance our field.

Message from the President

It is with great pleasure that I welcome you to this edition of the Neurosphere journal. As the president of King's College London Neuroscience Society, it has been an honour and privilege to work alongside our committee to serve the neuroscience community. Unlike the past 5 years, this year began afresh with an entirely new generation of committee members, but we have nonetheless excelled. This year we've seen an unprecedented 200+ engagements with our Fresher's fair stand in Old Billingsgate, a tripling in the number of social events delivered, and the formation of strategic partnerships with UCL Neuroscience Society and Hong Kong Student Association of Neuroscience to bring our members bigger and better events. As a member of our society, I hope that you've been able to partake in some of these fantastic events, and have found yourself a neuroscientific home. Looking forwards, I have complete faith that next year's committee will achieve even greater things, and that neuroscience continues to grow in King's College London.

Daniel Shao
Society President 2022/23

Message from the Editor in Chief

I wanted to extend my thanks to everyone who worked on this journal. It has been an incredible experience from start to finish. I have had the pleasure to work closely with everyone in the team, from seeing the author's plans materialise into first drafts, to seeing the editors work meticulously with their authors following the input of the peer reviewers. Everyone in the team has been absolutely fantastic, working so hard to put make this issue come to life, delivering it to the hands of our readers. Thank you for all your support! I look forward to launching the next issue this summer and hopefully seeing some of these contributors again, as well as new voices to join the team!

Alex Epshtein
Editor In Chief 2022/23

King's College London Neuroscience Society Committee 2022/23

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Neuroscience Rep Tharaniya Ganesalingam

Post-Grad Rep Ebru Ozkazman

Psychology Rep Alysha Lal Shewandas

ACADEMIC YEAR 2022/23

Joining the Neurosphere Student Journal

The Neurosphere Student Journal is King's College London's only peer-reviewed student scientific journal, and we're looking for neuroscience enthusiasts to write for our next issue! If this is you, why not get in touch with our incoming Editor-in-Chief and start writing for us? We are also on the search for editors and peer reviewers to join us, so please get in touch if you're interested.

Benefits of Joining

- Improve your own academic and scientific writing skills, which will be particularly useful for final dissertations or critical paper analyses in certain modules' assessments.
- Boost your portfolio with inside tips and advice for getting your own research works published in ISSN, ISBN or PubMed ID index publications.

Joining as an Editor

- As an editor, your role will be to mentor students through the scientific writing process from start to finish. This will include giving advice and feedback on article outlines, structure, literary research techniques and scientific writing style.
- Students must have prior works and author credits in established scientific publications that are either ISSN, ISBN, or PubMed ID indexed. You may also be asked for an example of your work.

Joining as a Peer Reviewer

- As a peer reviewer, your role will be to check that articles are methodically sound, factually accurate, and their sources are scientifically credible. Training can be provided.
- Students must be affiliated with either FoLSM or IoPPN, and hold an average grade equivalent to or above 65%

Editor-in-Chief(2022/23): Alex Epshtein
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SUBMITTING AN ARTICLE

Writer's Information Package

This writer's information package contains all the information needed to guide you through the writing process, which will see your finished article published in our Journal! To get started, please email the incoming Editor-in-Chief (contact details given below) from your King's, Imperial, or University College London email address.

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1. Article Outline

The first step is to draft an article outline. Unfortunately, the Journal is unable to accept pre-written articles or submissions from students outside of King's, Imperial, or University College London.

1) Before submitting an article, please send in an outline of the article you wish to write to our Editor-in-Chief (contact details below). Depending on the content or topic, they may assign you to work with a different member of the editorial team to best fit your needs.

2) Your outline will then be assessed, with any feedback returned to you. This process will repeat until an article outline is accepted.

3) A submission date will then be given to you for writing a draft of your article, along with an anticipated publication date.

4) Using the provided feedback, you may then start to complete your article draft.

5) Your completed article draft may require further revisions once submitted (see section 4. Article Acceptance).

2. Article Topic & Type

The Journal welcomes topics relating to basic, translational or clinical neuroscience. Topics that are clinical in nature (such as those on psychiatry, neurology, or neurosurgery), or based on scientific or medical education are also welcomed. Unfortunately, the Journal is unable to accept articles whose topics are on psychology, or articles written in an essay format.

Articles must be one of two article types:

- Literature Review (called *Research*)
  a scientific research article giving a methodical summary of the current understanding of a topic. These articles are usually researched from databases such as PubMED, and are structured with an abstract, introduction, methods, results and discussion, and conclusion.

- Commentary Article (called *Letter*)
  a commentary on systemic scientific or clinical practices or direction. Whilst these are more opinionated in nature, they must still be substantiated by significant research and evidence.

3. Article Content

Please keep the following in mind when writing:

- The preferred submission file format is Microsoft Word document (*.docx).
- Article titles should be no more than 2 lines on print, which equates to roughly 75 characters (including spaces) and should not contain any punctuation, abbreviations or acronyms.
- Content complexity should be aimed towards first year undergraduate students; that is, assume A-Level knowledge and a basic understanding of biological principles, but not the topic at hand.
- Word count is strongly recommended to be 750 words minimum excluding references, but there is no upper limit. For review articles we recommend 1000 words minimum excluding references and an abstract of 100 words.
- For review articles, please structure your article with an abstract and sections for the introduction, methods, result and discussion, and conclusion. The methods section should detail your literature search strategy and inclusion/exclusion criteria. Your editor will be able to advise you with your search strategy.
- Referenced material must be ISSN, ISBN, or Pubmed ID indexed.
- Citations should be made in numeric Vancouver style, with in-text citations being made with lower case square brackets enclosing the reference number.
- All abbreviations should be written out in full on the first mention, with the abbreviated form then given in parentheses.

4. Article Acceptance

Once your first article draft has been submitted, this is what you can expect to happen next:

- Your editor may give feedback and suggest minor revisions. These may relate to the article's structure, content, or writing style. Your editor will work with you collaboratively to get your article to publication standard.
- Once a final draft is accepted by your editor, it will be passed on to be peer-reviewed to ensure factual accuracy and scientific credibility.
- The peer-review team may pass feedback on to your editor, in which case further revisions may be needed and the article will be resubmitted for peer-review.
- Once your article has been accepted by both your editor and the peer-review team, your article will be ready for publication!

5. Article Publication

Once your article has been accepted, this is what you can expect to happen:

- The Journal is published once per semester on the Society's website. If your article misses that semester's submission deadline, it will be rolled-on to next semester's issue.
- Once published, feel free to share your article on social media!

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